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A PRACTICAL JOURNAL BUILT ON MERIT

EDITORIALS

INTRODUCTION

THIS Symposium of Obstetrics has been made possible by the support of the Editor of The American Journal of Surgery and the efforts and coöperation of the various contributors.

The field of obstetrics is assuming a constantly increasing importance in medical education and practice. This is true because it has come to be realized that there was and still is much unnecessary loss of health and life associated with the vital and essentially physiologic processes of human reproduction.

Ignorance and lack of adequate care due to many factors have played important parts in contributing to these disabilities and deaths of mothers and infants. It has been a controversial matter as to whether or not these results could be improved. This can be no longer a matter for argument as statistics now prove that the lives of mothers and newborn infants can be saved by disseminating knowledge and by providing more adequate care for women during pregnancy, labor, and the puerperium and for the newborns during the antenatal, intranatal and postnatal phases of their existence.

When the maternal mortality rate per 10,000 live births can be reduced from 69 in 1928 to 43.5 in 1938, the stillbirths from 39 in 1927 to 33 per 1000 live births in 1937 and the neonatal death rate per 1000 live births from 36.1 in 1927 to 31.3 in 1937, there is no longer a valid argument against the possibility of reducing the number of deaths.

It is apparent that the mortality rates can be improved by the general application of the knowledge we already have. It is still undetermined how great a reduction in deaths is possible. It has already been demonstrated in certain states that the general rate can be reduced 50 per cent, though thus far the rate for the registration area has been cut something over 25 per cent. There are local statistics showing that the maternal mortality rate can be reduced to as low a figure as 1 per 1000 live births and even less. It could reasonably be anticipated that with adequate consecutive care by competent personnel with essential equipment not more than one pregnant woman in a thousand need lose her life during the pregnancy, the labor and the puerperium.

There is an unnecessary loss of fetal and infant life which can be markedly reduced. The combined stillbirth and neonatal death rates now equal about 70 per 1000 live births. There is sufficient evidence to prove that with complete and adequate prenatal, natal and postnatal care these combined rates could be brought down to 35. What possibilities open up with the application of new knowledge requires a prophetic

instinct which cannot be based on any scientific data. While individuals are doomed to die ultimately there would seem to be little justifiable reason for a healthy woman to die while carrying out a biologic and physiologic process, nor would it seem necessary that the life of a fetus should be arrested in its incipiency. A great deal of discussion and thought has been given to the deaths which have taken place in connection with the carrying out of the function of human reproduction. Death is a very real and tangible affair which can be used as a basis for statistical computation. Morbidity is difficult to define, to estimate and to use for statistical comparisons. Many of the causes of death may produce disability of varying degrees and duration and unquestionably the improvement of the general level of obstetric care will in addition to saving lives, lessen the disabilities associated with childbearing.

Formerly there were many genital fistulas as the result of birth injury; now they are infrequent. Congenital syphilis is of less frequent occurrence than formerly and by generally adequate care can be eliminated. These examples are definite illustrations of what has been done and are positive indications of what can be accomplished.

In attempting to secure as nearly perfect results as possible it is necessary to realize that coëxistent diseases are affected by pregnancy and its sequelae and that the course of gestation is modified by these diseases. It is of the utmost importance to know the physical and mental status of the woman who is about to be or already is pregnant. We have chosen three diseases which are quite frequently seen and which have a very intimate interrelationship with reproduction and increase the hazards of childbearing. Women who have venereal, tuberculous or cardiac diseases require special attention and treatment even though no pregnancy is present, but when the two conditions coëxist the required attention is definitely increased. Even early pregnancy presents certain hazards which are inherent in the pregnancy itself. Ectopic pregnancy is a very critical condition and has to be recognized and treated promptly to avoid disaster. It is difficult to diagnose even when it presents acute symptoms of rupture. Stress upon its diagnosis with early institution of hospitalization and of surgical treatment are definitely in order. Abortion is a manifold problem both from medical and sociologic points of view. It is not possible to give accurate data relative to the annual number of abortions which occur in our country, but there must be 750,000 or so. Many of these are unavoidable with our present knowledge and they often cause much grief in a family desirous of having children. On the other hand the intentional abortions are numerous and they result, in many a fatality which could be avoided, and cause much disability and subsequent sterility from infection. Those women who desire children should accept a pregnancy when it comes and not attempt postponement to some more convenient time at the expense of fetal life and of a hazard of greater or less risk of death and of disability to themselves. The importance of prenatal care and preparedness is illustrated by the causes of obstetric hemorrhage. The well being of mother and fetus is promoted by observation of the maternal nutritional state and by supervision of diet under both normal and abnormal conditions.

Labor is the crucial period during which the fate of both mother and baby may be determined within a few moments. It is important that the doctor be sure of his ground and not yield to the importunities of relatives and patient for an easy or short labor rather than one safe for mother and infant. One cannot compromise judgment which involves health and life. Two lives hang in the balance and one should not tip the scales to cheat nature but so adjust them as to assist her. The Symposium continues to give a pictured outline of the normal and abnormal aspects of labor with some consideration of prevention and repair of complications such as hemorrhage and laceration.

Infections do arise and, while prophylaxis remains of the greatest importance, nevertheless great progress has been made in their treatment. The newborn cannot be regarded as an obstetric by-product, and if its fate is not determined during pregnancy and labor the first few moments of extrauterine existence may decide between life and death or between a normal and a handicapped existence. The establishment of respiration is vital but it should be normal. It is of little use to have breathing established artificially and then have death from pneumonia or pneumothorax follow a few days after.

No attempt has been made to present complete expositions of the various subjects included in this symposium to say nothing of writing a comprehensive document on obstetrics. We have tried to indicate the field covered and to outline some of the frequent and outstanding problems in present day obstetric practice.

Fred L. Adair, M.D.

THE CHANGING ASPECTS OF GYNECOLOGY

THE papers which are included in this Symposium on Gynecology may, I believe, be considered truly representative, not only from the standpoint of the authors but also as regards the topics which are discussed. Certainly they exemplify the changing aspects of gynecology, and emphasize the fact that it can no longer be considered a mere subdivision of surgery, as seemed to be the tendency not so many years ago. As a matter of fact, only a small proportion of gynecological patients nowadays are in need of surgical procedures. Sometime ago I happened to sit in on a discussion of this very point by a group of prominent gynecologists. All agreed that the proper management of most gynecological cases does not call for surgery, none placing the proportion of surgical cases above 10 per cent, and most of them at considerably less.

A large proportion of our nonsurgical patients, though not by any means all, are those presenting various functional disorders, especially of endocrine nature. The development of gynecological endocrinology and the increasing interest in the general biologic aspects of our specialty constitute the most outstanding contribution of the present generation to gynecology. Just as the preceding era was characterized by an awakened interest in the pathologic aspects of gynecological disease, and a still earlier one by that remarkable development of gynecological surgery to which subsequent years have added so little, so may we now properly consider ourselves in a physiologic or biologic era of gynecology.

Both pathology and surgery are still, as they will always be, of fundamental importance in the training and practice of the gynecologist. Not all the surgical and pathologic problems of our specialty have been solved, and some of these, such as the applicability and technique of vaginal hysterectomy, the still much discussed question of total versus subtotal hysterectomy, and the early diagnosis of cancer are discussed in this symposium by outstanding authorities.

In the same way, the fascinating and intricate though as yet imperfectly understood problems of gynecological endocrinology are presented by authors selected because of their contributions and accomplishments in this potentially rich new field.

One does not need to be an old man to reminisce on the amazing advances which have been made during the past generation in our knowledge of the physiology of the reproductive cycle. It seemed so simple to our immediate forbears to explain menstruation as due to an internal secretion of the ovary, though this explanation seemed rather nebulous since nothing was known as to the source or nature of this secretion. Now, on the other hand, our concepts are

made concrete by the fact that both of the ovarian hormones have been isolated, that we know the exact chemical composition of both, and that both can be prepared in crystalline form, so that they can be handled much as we handle drugs, especially since we know a good deal as to their physiologic effects.

We have learned much too, as to the interrelationship of ovarian function with that of other endocrine glands, especially the pituitary, so that we no longer conceive of the menstrual cycle as a purely pelvic phenomenon, but think of it rather as embracing far-flung and deeply seated constitutional changes, which include certain conspicuous pelvic phenomena whose ultimate purpose is the propagation of the race. In the study of all the cogs in this complex machinery there have been rich opportunities for the clinician, the anatomist, the physiologist, and the biochemist, and all have made rich contributions. And yet there is a general feeling that the surface has been merely scratched and that many rich nuggets will be uncovered by the intensive work now being devoted to all aspects of the general problem.

No apology seems necessary, therefore, for including in this Symposium a considerable number of papers devoted to the consideration of functional or endocrine problems, particularly in view of the authoritativeness of these presentations. The other topics have all been selected because of their present day interest, and all are discussed by writers whose names are identified with the subjects which they present. If this number of The American Journal of Surgery is read by one of our successors a hundred years hence, it should convey a correct picture of the type of gynecological problems which engage the interest and attention of the gynecologist of today.

Emil Novak, M.D.

OBSTETRICS AND GYNECOLOGY SYMPOSIUM

OBSTETRICS

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PRECONCEPTIONAL CARE

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PRECONCEPTIONAL care is designed to assist in securing perfect reproduction. It rests upon fundamental eugenic and euthenic principles. It is that care and attention which is given prior to conception and involves the elimination of those individuals who are not suitable for wholesome reproduction and the selection of those who are capable of normal reproduction. This elimination and selection must be based on known biologic principles which can be best adapted to humanistic, ethical, social and economic customs and laws. The application of the principles must fit into the legitimate and proper needs and desires of individuals and of society. It is a part of complete maternal care, but includes the examination and care of both the male and the female. After conception occurs the essential attention involves primarily the prospective mother and the fetus during pregnancy and labor, and of the mother and newly born infant as more or less completely independent individuals. One may, therefore, include the entire program under the general title of Maternal Care or Welfare, as the mother is the keystone of the complete arch of human propagation.

In defining Maternal Care it must be borne in mind that in order to be complete and competent the attention given to the mother must be such that it will both directly and indirectly enable her to carry out the physiologic process of reproduction in as nearly normal a manner as possible. This implies the maintenance of the integrity of the family and insures the reproduction of normal offspring in sufficient numbers to preserve the human race and promote its advancement.

In order to secure a survey of the field of endeavor and place preconceptional care in its proper sphere, it is important to understand the different phases of the program of Maternal Care.

1. Preconceptional care includes all the eugenic and euthenic attention which is necessary to determine the fitness of individuals to bear children and to prepare them for conception and to protect the offspring, during both intra-uterine and extra-uterine life, from detrimental influences which might subsequently interfere with a normal and reproductive life.

2. Antenatal, prenatal and antepartum all refer to the care given to the prospective mother and to the fetus during gestation. The first and second terms refer more specifically to the fetus while the last one designates the mother as the particular object of attention.

3. Natal, intranatal, intrapartum and delivery care apply to the care and attention given to the mother and the fetus during labor. The first two words refer more particularly to the welfare of the fetus and the latter two terms apply to the mother. Usually their interests are mutual, but sometimes they are in conflict.

4. Postnatal and postpartum care are quite distinct in that the mother and the infant become independent individuals. The care is quite divergent and while the two live in a sort of symbiosis they are physically separate from one another. This independence normally develops progressively as the weeks, months and years pass. The care of both may be divided into the immediate and the remote. With regard to the mother this postpartum care immediately assumes an aspect which is related to preconceptional care. It is important that, among other things, she be left with a desire and a capacity subsequently to carry out a normal reproductive career.

With reference to the newborn it is important to bear in mind that its growth and development carries the implication that the normal individual must be able at the proper time to reproduce normal human beings, and if possible those who are of a superior rather than of an inferior quality.

It is obvious that adequate Preconceptional Care involves a consideration not only of the potential fathers and mothers, but also of their individual progenitors. It is apparent that it includes both eugenic and euthenic backgrounds. It must be understood to include within its scope both the present and the future welfare of humanity and that the good of all is paramount to that of the one or of the few. It must sooner or later be recognized and acknowledged that it includes within its scope both contraception and proconception and that it is oftentimes as important for the welfare of one or of all to avoid conception as it is to promote conception. We should reconcile our minds and our acts to the idea that ultimately the birth rate will have to be judged not alone on a quantitative but also upon a qualitative basis. Our major concern will ultimately be not solely whether the birth rate exceeds or equals the death rate, but also whether or not the quality of those who are born and survive is better than that of those who succumb.

It is a well known fact that there has been a downward trend of the birth rate for a number of past decades. There is little evidence to support the idea that this is due to decreased fertility. The statistical data seem to indicate that just as many women are capable of reproducing but that the number of pregnancies per woman has diminished. Some studies have been made to determine which social groups tend to reproduce the fewest, and it appears that the intellectual and higher economic groups tend to have the smallest number of children. Some have argued that there is a tendency for the human race to become biologically inferior. It is very difficult, except in smaller groups of defective individuals, to erect biologic criteria of fitness. Most of the analyses of the birth rate have been on a quantitative rather than a qualitative basis. Both are important as the live births must equal or exceed the deaths, or the human race will ultimately become extinct.

The quality is important as it must equal or exceed the present, or the human race will deteriorate. What qualities must be preserved and transmitted? They cannot be those which frequently make for economic success or for failure, as those who become rich may have undesirable qualities and those who are poor possess desirable ones. They cannot be solely intellectual as one may be brilliant and be intellectually perverted. They cannot be purely physical as one may be a giant in body but a pigmy in mind. Society is very complex in its organization, and there must be those who can fit into the different niches and carry out their functions adequately.

What should one consider as the essentials in those who are to provide the future componenets of the human race? First, they should be physically fit by being free from hereditary and transmissible diseases. Second, they should be mentally fit to understand and adapt themselves to life in the community of their fellows. Third, they should have character to withstand the harmful temptations of life and a willingness to work with and help their fellows rather than to profit by their exploitation.

How to accomplish these objectives is quite another matter, but beginnings are being made and gradually one idea after another will be applied and eventually the desired ends will be accomplished. We have started with the physical side first and real attempts are being made by means of premarital examinations to avoid the transmission of disease to the partner and to the offspring. More and more parents are coming to realize that good health is important, not only during pregnancy, but also at the time of conception. The application of these ideas involves two basic principles. First, the avoidance of concep-

tion at any time in those who are not adapted to normal reproduction. Second, the prevention of conception in those who are temporarily not suited for normal propagation.

At present our basis of selection rests almost entirely on physical or medical grounds. The doctors and other scientists, therefore, must assume the responsibility for this very important program of human welfare. As already indicated the decision rests upon certain eugenic and euthenic principles which have been established. One cannot and should not proceed upon theoretical considerations. Individuals with known serious hereditary defects should not reproduce their kind. Perhaps the steadily increasing stream of defectives could be arrested by this means. Transmissible disease such as syphilis could certainly be eliminated. Health and longevity could be promoted by timing a pregnancy, as in a tuberculous woman.

The methods become of importance, and obviously different procedures would be indicated for permanent and for temporary contraception. Sterilization is most appropriate for the former and contraceptive devices for the latter. The rhythm theory limits the number of gestations but is not to be relied upon in those for whom pregnancy must be interdicted either temporarily or permanently. The use of obstructive devices with or without chemical spermatocides is successful where they are properly applied and consistently employed. Chemical contraception has not attained perfection and various agents for the purpose of arresting spermatogenesis are not yet satisfactory. It must be remembered that some devices are seriously harmful and disability and even death have resulted from their use.

Sterilization of the male or the female is a relatively simple procedure especially in the former, although males are difficult to convince that cutting the vas deferens is simple, safe and harmless. They are more willing to have their wives suffer an abdominal incision with ligation of the tubes. The lumen of the tube may be occluded by a variety of methods from cauterization, ligation, resection, excision and even hysterectomy. These procedures may be carried out before any pregnancies have taken place or after one or more have occurred. They may be done to prevent the birth of a potentially defective fetus or purely in the interest of the mother's health and life.

The interruption of a pregnancy hardly should be incorporated in a discussion of preconceptional care, but a therapeutic abortion frequently presupposes that a future pregnancy is also undesirable.

It seems consistent to follow the principle that when the pregnant woman is suffering from a persistent disease which necessitates a therapeutic abortion, she or her husband should be sterilized. This would avoid the necessity for a future abortion. The solution of such a problem arises in chronic cardiac, vascular and renal diseases. If the condition is acute and recovery probable, sterilization is not indicated, but contraceptive devices should be used until recovery is complete and pregnancy safe.

Preconceptional care has been discussed from the standpoint of control of reproduction but the opposite point of view is even more important. This may be termed the proconceptional viewpoint. There are two main groups of cases which come under consideration here. First, those who are presumably capable of reproduction and, second, those who have been unable to have children.

No discussion will be given of the infant, child and adolescent care, necessary for the growth and development of normal persons, which will be assumed to have been obtained. The result should be two presumably healthy young adults contemplating marriage and the founding of a family. They come for a prenuptial or a premarital examination. Such a requirement has the force of law in some states. The law which became effective in Illinois on July 1, 1937 is quoted in the following paragraphs:

"*Section* 1. Section 6a of 'An Act to revise the law in relation to marriage,' approved February 27, 1874, as amended, is amended to read as follows:

"Sec. 6a. All persons making application for a license to marry shall at any time within fifteen (15) days prior to such application be examined by a physician duly licensed in this State as to the existence of or freedom from any venereal disease, and, except as otherwise herein provided, it shall be unlawful for the county clerk of any county to issue a license to marry to any person who fails to present for filing with such county clerk a certificate signed by such physician setting forth that such person to the proposed marriage is free from venereal diseases as nearly as can be determined by a thorough physical examination and such standard microscopic and serological tests as are necessary for the discovery of venereal diseases. If, on the basis of negative laboratory and clinical findings the physician in attendance finds no evidence of venereal diseases, he shall issue a certificate to the effect to the examinee, which certificate shall read as follows, to-wit:

"I, (Name of Physician) _____ being a physician, legally licensed to practice in the State of _____ (my credentials being filed in the office of _____ in the City of _____ County of _____ State of _____) do certify that I did on the ____ day of _____ 19____ make a thorough examination of _____ and considered the result of a microscopical examination for gonococci and an approved serological test for syphilis, which was made at my request, and believe _____ to be free from all venereal diseases.

_____

Signature of Physician

"Such certificate of negative findings as to each of the parties to a proposed marriage to which laboratory reports of microscopical examinations of smears from the genitalia for the gonococcus of gonorrhea and serologic tests for syphilis are attached, shall be filed with the county clerk of the county wherein the marriage is to be solemnized at the time application is made for a license to marry. Laboratory tests for venereal diseases required hereunder shall be tests approved by the State Department of Public Health and shall be made by laboratories of said Department or by such other laboratories as are approved by said Department. Such tests as may be made by the health departments of cities, villages and incorporated towns maintaining laboratories shall be free of charge. The results of all laboratory tests shall be reported on standard forms prescribed by the State Department of Public Health.

"Irrespective of the results of laboratory tests and clinical examination, the clerk of the respective counties shall issue a marriage license to parties to a proposed marriage (a) when the woman is pregnant at the time of such application, (b) when the woman has, prior to the time of application, given birth to an illegitimate child which is living at the time of such application and the man making such application makes affidavit that he is the father of such illegitimate child. The county clerk shall, in lieu of the health certificate required hereunder, accept, as the case may be, either an affidavit on a form prescribed by the State Department of Public Health, signed by a physician duly licensed in this State, stating that the woman is pregnant, or a copy of the birth record of the illegitimate child, if one is available in this State, or if such birth record is not available, an affidavit signed by the woman that she is the mother of such child.

"Also irrespective of the results of laboratory tests and clinical examination, the clerks of the respective counties shall issue a marriage license to parties to a proposed marriage when, after investigation, the Director of the State Department of Public Health, or his duly authorized representative, issues or causes to be issued a certificate that such marriage may be consummated without serious danger to the health of either party to the proposed marriage or to any issue of such marriage.

"Any county clerk who shall unlawfully issue a license to marry to any person who fails to present for filing the certificate provided for in this Act or who shall refuse to issue a license to marry to any person legally entitled thereto under this Act, or any physician who shall knowingly and wilfully make any false statement in the certificate, or any party or parties having knowledge of any matter relating or pertaining to the examination of any applicant for license to marry, who shall disclose the name, or any portion thereof, except as may be required by law, shall upon proof thereof be punished by a fine of not less than $100.00 nor more than $500.00 for each and every offense.

"Any person who shall obtain any license to marry contrary to the provisions of this section shall, upon conviction thereof, be punished by a

fine of not less than $100.00 or by imprisonment in the county jail for not less than three (3) months or by both such fine and imprisonment. Any license to marry issued hereunder shall be void thirty (30) days after the date thereof."

It is to be noted that this law is primarily directed toward the control and elimination of venereal disease. The law is an admirable beginning and does focus attention on certain health problems in relation to marriage. It falls far short of what should be considered essential for preconceptional and premarital examinations. An adequate investigation of this type should include a study of both prospective parents from standpoints of their heredity, of past diseases and of the present state of their health. This includes a complete history and physical examination with routine laboratory tests and special studies when indicated.

It is not fully known just what influences affect the germ cells during the process of their development and there are enormous gaps in our knowledge of human heredity. We know that certain agents can destroy the male germ cells, and it is fair to assume that the same or similar agents can injure them but probably not entirely destroy their fertilizing power. It is well known that there are many embryonic and fetal malformations and that the examination of semen of different males shows varying percentages of normal and abnormal, mature and immature germ cells. Little is known about the fertilizing power of these various types of germ cells and of the ultimate result so far as any resultant embryos are concerned. The routine examination of this secretion is not indicated but it should be done in cases of sterility, abortions and malformations. It is, of course, impossible to secure ova for examination, but modern methods show the possibility of drawing certain conclusions relative to anovulatory cycles by endometrial biopsy. The ovaries are well protected from external influences; however, toxic and infectious agents gaining access to the maternal blood stream may affect their formation and development temporarily or permanently. The male gonads being more exposed are more susceptible to environmental influences. It has been shown that elevation of local temperature may affect spermatogenesis. It is an interesting question which should be answered as to what effect fever has on the development of ova and sperms.

This discussion indicates the importance of considering illness in relation to conception and it is not overdrawn to emphasize the importance of the parents being in good health prior to and at the time of conception. It is well known that infertility is frequently associated with poor thyroid function and that calcium and phosphorus and iodine have a relationship to productivity. If sterility can result from metabolic disturbances of this type it is only logical to assume that lesser damage to germ cells may occur and a poor offspring result. The main points of this discussion are that as a part of preconceptional care one should consider the facts that germ cells carry inescapable hereditary factors and that even though they lie protected in body tissues they are still susceptible to environmental influences.

After fertilization occurs the fate of the embryo is in part determined and the hereditary die is cast. Environmental influences can modify its intra-uterine development. The further course of development depends upon maternal environment. Preconceptional care strives to remove these detrimental factors prior to fertilization of the egg. There is no evidence that syphilis affects the male or female germ cells or that it is carried by them. The maternal environment is such that the treponema is carried to the fetus and infects it. The preconceptional diagnosis and treatment of syphilis will yield better results than recognition and care during the prenatal period. There is evidence in Connecticut and Illinois that the prenuptial tests are reducing the number of cases of congenital syphilis. Similar laws in

New Jersey, New York, and Pennsylvania will, no doubt, yield worthwhile results in controlling congenital syphilis. The transmission of syphilis from one partner to another is also important, irrespective of the possibility of the subsequent infection of the fetus and newborn.

The prevention of marital spread of gonorrhea is an even more difficult problem because the criteria for diagnosis and cure are less definite and the treatment is less specific.

Gonorrhea is not held responsible for as many fatalities as syphilis, but its ravages are not less great. The frequency of marital transmission is high and the incidence of subsequent male and female sterility as a result of its invasion is considerable. What effect it has as an etiologic factor in abortions has not been evaluated clearly, although the lesions of the cervix, corpus and tubes must be factors in the production of abnormal gestations. The amount of disability resulting in women from gonorrheal infections is very great, while the loss of reproductive function is usually irreparable and contributes largely to acquired sterility.

The other venereal diseases are less of a problem as they are limited to certain groups and, though serious in the individuals afflicted, the number of those infected is not great and the diseases are not widespread. There are also communicable diseases other than these whose transmission from one mate to another can be controlled by preconceptional care. The acute infectious diseases are usually transient and more or less general in their distribution so that only commonly recognized methods of control can be of any avail. However, such a chronic infectious disease as tuberculosis may be unrecognized even in its active contagious stage, and a man may infect his bride or she transmit the disease to him. It is important that pulmonary tuberculosis be diagnosed so that proper precautions may be taken before the hazards of marital life transmit the infection from one to the other. It is particularly important that no woman who has an uncured tuberculosis should become pregnant.

Preconceptional care has to do with the elimination of those conditions which cause infertility or tend to reduce fertility. These involve the careful examination of both male and female and even then cases are relatively frequent in which no definite cause can be determined. However, the more careful and thorough the examination the fewer the unexplained cases will be. It does not follow that, even though the cause is determined, the remedy is at hand. This is particularly true of the obstructive forms of sterility where either the male or the female passages are closed for the transport of the germ cells. Either one or both partners may be involved in this type of sterility. The finding of an aspermia in the male may be due to a lack of development or to an obstruction. The former may be susceptible to remedy or may be incurable, depending upon the cause. The latter may be remedied by a delicate and not too successful operation for anastomosis. It is difficult to determine in the female whether or not ova are formed, but usually the condition of the passages can be diagnosed by various tubal patency tests. If the tubes are occluded there are various types of operations, usually unsuccessful, which may be done in properly selected cases upon the insistence of the patient.

When the male is proved sterile, but his wife is not, the question of artificial insemination may arise. At present the ethical and legal status is not clearly defined. It is usually the wife who takes the initiative in the attempt to discover why she is barren. Most husbands are willing to coöperate by submitting to an examination, but some are not. Of course, there are some women do not desire to bear children.

Sometimes the history will disclose the probable cause of the female sterility and such facts as pertain to general health, evidence of disordered endocrinal or metabolic functions as of the thyroid, symptoms indicative of genitourinary disease should be ascertained. Habits of life, especially of sexual life, are important. What effect

perversions and long continued use of contraceptive methods may have on reproductive power is not known. It seems that too frequent indulgence may reduce fertility, especially in the male, and that sedentary, inactive physical life with increased weight, etc., may be a factor. The diet may be of importance and dearth of certain minerals, vitamins, etc., may be responsible for an inability to procreate.

Many of these facts can be gleaned from the history, but a careful physical examination with the necessary laboratory tests should be done. Just what these should be varies with the individual patient. There should be a general physical examination by which some pertinent facts may be discovered and also the fitness of the woman to bear children be determined. The obstetric and gynecologic features of the examination should be carried out in detail. A Hühner test should be done to determine the presence and potency of the sperm cells and, if possible, to see whether or not the genital secretions are harmful to them. It is rarely necessary to inseminate the wife artificially with her husband's semen.

The husband should be examined physically and his seminal discharge studied for presence or absence of sperms, their motility, form, maturity, etc. The presence of adventitious cells should be noted. Blood and pus cells are at times found. Impotency may be present. Neurologic diseases in either or both partners have to be discovered as they may have a bearing on the solution of the problem. The determination of the basal rates of the woman should be routinely done and any evidence pointing to a deficiency on the part of her husband should be proved by a basal metabolic test on him. Endocrinal assay and its significance is not sufficiently well established in accuracy or in experience to justify the setting forth of any positive statements. It is probable that ways and means of stimulating normal ovulation and spermatogenesis may be perfected. The timing is important, as most of the evidence indicates that the life of the ovum is short and that the spermatozoa do not survive long in the female genital tract. Ovulation is at its peak between the ninth and fifteenth postmenstrual day. This is subject to great variation in different individuals and even in the same woman at different times and under varying conditions.

The possibility of estimating the time of ovulation in a woman by delicate electrometric methods is a real one. Such a procedure would be of value in determining whether or not a patient ovulates and if so how often and at what period of the cycle.

SUMMARY AND CONCLUSIONS

This survey gives a general idea of some of the problems involved in the many aspects of preconceptional care. Fundamentally it involves the education of the physician to its importance and to its application and of lay groups as to its desirability and to its value to them and to society. It will be difficult to force the matter by law unless it is backed by popular opinion. This is evidenced by the fact that many couples migrate from districts imposing legal restrictions and are married in areas not subject to premarital laws. In some states having these laws the marriage rate has declined. The purpose back of the law is good, but the people must realize its value. The law is justified by the importance of preventing the spread of communicable disease by marriage. There are, however, many other very important aspects which laws could not now, or possibly ever, encompass even if the passage of such far reaching legislative regimentation were desirable. Education to the importance and value of preconceptional care will suffice for those who have sufficient intelligence to comprehend its significance for them and for society. For unintelligent and recalcitrant individuals other methods than educational will doubtless become effective. Again, the medical profession is called upon to recognize and to lead in the educational and technical sides of this program designed for human health and welfare.

RELATION OF VENEREAL DISEASE TO OBSTETRICS*

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SYPHILIS and gonorrhea are the two leading characters in the drama of venereal disease in association with pregnancy, the former because of its villainous nature and the latter because of its treacherous behavior. The three other venereal diseases, chancroid, granuloma inguinale, and lymphogranuloma venereum are distinctly less serious because of their actual infrequency, their usual and likely conspicuousness, and the relative safety for the fetus.

Particular points of interest are: the alteration in the course of the disease because of a pregnant state; the effect the disease has upon the product of conception; and the complications in labor and the puerperium. Since the behavior of each of the venereal diseases may be as unpredictable as a malcontent, separate discussions ensue for each clinical entity. Actually one might consider the effect of these diseases upon sterility, abortions, stillbirths, intrauterine infections, arthritis, endocarditis, central nervous system diseases, dystocia, conjunctivitis, puerperal infection, etc., in detail. However, the present diagnostic methods, prophylactic measures, and efficient and sane therapies can stand review in light of the inadequate obstetric care that many patients still receive in the United States. Certainly part of this responsibility lies with the patient for lack of coöperation with her obstetrician, but more likely this reflects the failure of the physician and especially the obstetric leaders in those communities to "educate" the laity to the virtue and value of proper, adequate and intelligent preconceptional, prenatal, natal and postnatal care.

SYPHILIS

Syphilis, a deceitful tricky disease, is the most important of the venereal diseases in association with pregnancy. It is sneaking and tricky because after the secondary stage is over the latent third stage may pass quietly and without symptoms. Many a syphilitic pregnant woman has had stillborn or living luetic babies before any obvious clinical evidence appeared. Parran[1] estimates that 60,000 congenitally syphilitic children are born annually. The actual number of syphilitic mothers giving birth to nonsyphilitic babies yearly due to adequate therapy during the pregnancy is problematic. Surely the number is large.

The etiologic agent and means of spread are well established. Diagnostic serologic methods are available to all practitioners, but unfortunately not all of the profession make use of these tests in each pregnancy and as early as possible in the course of the pregnancy.

The ideal practice of premarital tests for venereal diseases, especially syphilis and gonorrhea, cannot be overstressed, as it makes possible proper therapy before conception. If every pregnant woman came under the care of her physician early in the first trimester and every physician excluded then the possibility of venereal disease in the patient, congenital syphilis could be almost completely eradicated.

Usilton, Hunter, and Vonderlehr[2] found that in one-half of the women syphilis was undetected before the fifth month of pregnancy. At this same time nonsyphilitic women had a stillbirth rate of 2 per cent while syphilitic women had 10 per cent

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incidence. With treatment this latter rate declined to 5 per cent.

Leading obstetricians and syphilogists agree with McCord,[3] and Beck and Daily[4] that every pregnant syphilitic woman should have adequate and active antisyphilitic treatment throughout pregnancy. McCord, in a series of over 3,000 syphilitic gravid women, found that without treatment 35 per cent of pregnancies ended with a healthy living baby, while with treatment 95 per cent of the gestations terminated in healthy uninfected babies. He elaborates further that in every syphilitic baby there should be placental syphilis even though it is not demonstrable. It is generally accepted that transmission to the fetus takes place probably sometime after the placenta is well developed. If this correct, then treatment started by the end of the first trimester should offer the unborn child a good protection. Treatment should be begun whenever the diagnosis is made even though it is late in pregnancy. This is justified because there is a possibility that the fetus has not yet become infected (probably infrequent) and also to institute treatment for the fetus if it is diseased.

Cord Wassermanns may be negative in 37 per cent of syphilitic infants according to Cooke and Jeans.[5] Positive cord Wassermanns are more significant but may be misleading. Every infant of a syphilitic mother should have careful pediatric study to exclude or establish the diagnosis of congenital syphilis and should be followed for years. *X*-ray examination of the long bones for typical lesions should be a routine.

Another reason for administering therapy during pregnancy is that the maternal disease responds well at that time. It is true that rarely a complication contraindicates therapy, yet when it does, the situation must be carefully studied. Definite and severe kidney lesions may be one reason but not necessarily so. An occasional patient reacts unfavorably to arsenicals or is unable to tolerate the therapy. With careful management of each case, intolerance and complications are less likely to occur. Plass and Wood[6] report that "Pregnant women are more susceptible to the deleterious as well as the beneficial effect of antisyphilitic therapy by modern arsenicals." Due to this susceptibility most syphilologists adjust the dosage and alter the routine of therapy somewhat to fit into the pregnant state. Syphilitic therapy should not be administered until a positive diagnosis has been made.

The typical primary genital lesion of syphilis has a diameter of a few to several millimeters, a necrotic-like membrane on the cup or saucer-shaped ulceration, an encircling leathery or semicartilaginous induration, little or limited hyperemia, and practically no tenderness. The secondary stage is associated with multiple lesions on the skin turning copper-like on fading, and mucous patches in the oral cavity. The spirochete of syphilis may be observed in the serum from the primary or secondary lesions by means of dark field illumination. Since the third stage is a silent period (one without symptoms and quite often without clinical findings) the diagnosis must be made through the use of serologic tests done in certified and approved laboratories. Condylomata with a flat topped wide base on the genitalia suggest that syphilitic infection exists or has existed. Impaired knee and pupillary reflexes give indication of nervous system syphilis.

Every pregnant woman should have serologic blood specimens taken on the first visit. Most places use 10 c.c. more or less for blood Wassermann and Kahn or other serologic tests. After the completion of the general history, physical and obstetric examination and routine laboratory tests the patient should return in one week for further advice and possible "check." If the serologic tests are positive or questionably positive, a second test must be made. Becker and Muir at the University of Chicago Clinics treat every pregnant woman if she has had syphilis, even though she may be asymptomatic (regardless of the serologic reaction). At the Chicago

Lying-in Hospital therapy is begun with four weekly injections of 1 c.c. bismuth salicylate and followed with first 0.3 and then 0.45 Gm. neoarsphenamine. This is three-fourths of the regular adult dosage. This arsenical treatment is given weekly for eight weeks followed by five weeks of bismuth salicylate 1 c.c. and then continued in this rotation. These courses may overlap and a definite plan to alternate is made so that neoarsphenamine is given in the last month of the gestation. An exception is made in early syphilis when arsenical preparations are administered first.

GONORRHEA

It is generally assumed that gonococcal infections are of little import to pregnancy. Vonderlehr and Usilton[7] estimate that approximately 230,000 potential mothers in the United States acquire gonorrhea annually. No reliable data are at hand to show what percentage have gonorrhea and pregnancy combined. In the past enough babies developed gonorrheal ophthalmia from their infected mothers to cause many states to pass laws requiring prophylactic treatment to the eyes of every newborn.

Gonorrhea may cause sterility through damage or injury to the uterus, tubes, and/or ovaries. (Sterility or nonfertility is caused by many conditions other than gonorrhea.) Tucker, Trussell, and Plass[8] cultured gonococci from 4 per cent of pregnant clinic patients, one-half or 2 per cent of whom were asymptomatic and gave a "negative history." Such data alone indicate the need for more careful scrutiny in pregnancy for gonococcal infections. As pregnancy advances, and especially with local treatment, the lower genital tract may become normal in appearance and smears become negative for the gonococcus. Yet, an acute exacerbation may take place in the early puerperium.

After the first trimester of pregnancy, spread to the tubes is hindered because the sac of the ovum fills the entire uterine cavity. Spread to the heart, joints, and kidney may take place at any time in pregnancy, yet such complications appear no more likely during pregnancy.

After delivery the gonococcus has an open avenue again to the tubes and the peritoneal cavity. It has been said that postpartum gonococcal peritonitis is more likely a late complication. The disease pursues a course not so different from that in the nonpregnant.

The gonococci attack the urethra and cervix readily and remain in these sites, producing congestion, edema, hyperemia, and tenderness. Healing or recovery is a gradual process. Irritation on urination subsides slowly. The mucopurulent rich creamy discharge may become replaced by various vaginal discharges, the result of secondary invaders. The typical leucorrhea in vaginal trichomoniasis is bubbly, but otherwise the same rich creamy color. The vaginal walls may show evidence of infection in gonococcal infections too. Occasionally Bartholin's glands are invaded. Smears and cultures should be made from the material within the urethra, expressed from the urethral glands by pressure on the vaginal side. Urination should not immediately precede the examination. Vaginal material in the adult is less satisfactory for smear and culture studies. It is all the more important that the cultures and smears be properly taken from the urethra, cervix and the Bartholin's glands.

Bartholin's gland abscesses occur more often in association with gonorrhea than other infections. The treatment is drainage by incision. Cyst formation is not necessarily the result of gonococcal invasion, but during pregnancy only these cysts should be removed when symptoms or increase in size justify it.

Formerly condylomata acuminata or verruca acuminata were looked upon as definite earmarks of an existing or a previous specific venereal infection, but this is now known to result from several conditions, one of which is gonococcal infection.

For the product of conception there is no risk, aside from unintentional abortion

because of an endometritis or ectopic pregnancy due to tubal damage, until the membranes rupture. At the time of delivery, however, the eyes or genital tract may become inoculated. The infant's genital tract is so infrequently infected that prophylactic measures are not prescribed. In sharp contrast, the eyes offer an unusually fertile nidus which explains the importance of proper care of the conjunctival sac of the newborn.

Whenever there is any suspicion of the infection, smears and cultures should be made. McLeod's medium or a satisfactory substitute is recommended. Adair, Hesseltine, and Hac, with Taylor and Hibbs and their associates[9] have used this medium successfully even in Chicago winter climate for transporting the culture by trolley or car for a few miles in aerobic state (reasonable care is used to prevent pronounced chilling).

The oxydase reaction using a 1 per cent dimethylparaphenylenediamine or tetranmethylparaphenylenediamine hydrochloride facilitates in the selection of colonies in heavily mixed or contaminated plates. False positive reaction may be given by *B. coli* and *B. subtilis*. Meningococci and some of the neisseria subgroups as catarrhalis or flava, may also give the same reaction. Sugar fermentations identify these properly.

	Fermentation with Acid Formation			
	Levulose	Dextrose	Maltose	Sucrose
N. gonorrhea	—	A	—	—
N. intracellularis	—	A	A	—
N. catarrhalis	—	—	—	—
N. sicca	A	A	A	A
N. flava	A	A	A	—

Gonococcal cultures grow dependably in reduced oxygen tension. This may be accomplished by displacing the air with carbon dioxide from the encased petri dishes in special containers.

Carpenter, Leahy, and Wilson[10] stress the value of cultures over smears. The findings at the Chicago Lying-in Hospital are in accord.

Therapy is in a transitional state. Until recently only local therapies (there are several) and increased heat (locally or generally) were in good repute for the adult. The induction of general hyperpyrexia for a few to several hours is a serious undertaking and is contraindicated in association with complications or pregnancy. Local hyperpyrexia is of questionable merit particularly at present.

For a few years estrogenic hormone was employed generally for vulvovaginitis of the immature female.

Sulfanilamide therapy has replaced the other therapy but still fails to cure all. Most workers advise 60 gr. daily (15 gr. doses at four hour intervals) for five to seven days, then gradually decreasing to 45 gr. (four divided doses at four-hour intervals, 10-10-10-15 gr. each) for two weeks or longer. The patient must be observed frequently for drug reaction or intolerance (agranulocytosis, anemia, dermatitis, fever). Sulfapyridine has been recommended by some workers. A total of 45 gr. daily (15-7½-7½-15 gr.) at four hour intervals for two days, with a decrease to 30 gr. (7½-7½-7½-7½) at four hour intervals for five days. These patients must be observed carefully also.

CHANCROID

Chancroid infection is a localized disease, almost always found on the genitalia and caused by the Ducrey bacillus (*Haemophilus ducrey*). It produces as a rule a less indurated, or soft chancre. Inguinal lymphadenopathy is common, and one or more glands may suppurate. The various reports do not mention pregnancy in conjunction with this clinical entity. Hence there must be a relatively or actually insignificant occurrence in association with the gravid and parturient states. In the first place, chan-

croid is not a common condition and in the second place, there is rarely, if any, residual damage which might cause dystocia or be associated with other complications of parturition. Thirdly, this disease is a local process and runs a self-limited course. Thus there is slight chance of fetal or newborn infection. Whether the course of the disease is altered by the pregnant state or responds differently under this condition to therapy is unanswered. The only prophylactic measure for the fetus would be the usual cleansing at birth and the application of a non-irritating skin antiseptic. Perhaps ammoniated mercury ointment might serve the purpose.

The diagnosis may be made by finding the Ducrey bacillus (*Haemophilus ducrey*) with Gram's stains in scrapings from the primary lesion and in aspirated pus from the buboes. This organism, a streptobacillus type, may grow in defibrinated blood infusion agar (Torpin and Dienst[11]). Cole and Levin's[12] inability successfully to culture the organism justifies their stress on the specificity and value of the intradermal test. A foreign preparation (Dmelcos vaccine) or mixture of killed organisms and serum containing antibodies (which is barred from the United States) gives dependable results diagnostically. The positive intradermal test causes an infiltrated papule from 0.5 to 1. cm. in diameter in twenty-four to seventy-two hours. The induration is distinctly larger and the lesion may terminate in necrosis.

Sanderson, Greenblatt and Baethke[13] found the complement fixation test unreliable because of false positive reactions.

Since the reaction may persist for thirty or more years (Cole and Levin) a positive test does not prove conclusively that the lesion in question is necessarily chancroid.

Without specific reports or observations it seems that neither pregnancy nor chancroid alters the other's course. Apparently the fetus is not especially endangered and apparently therapy would not be contraindicated in pregnancy or the puerperium. Secondary bacterial invasion in draining sinuses must be a serious complication during parturition and the early puerperium.

Therapy consists of local hygienic measures and repeated aspiration of suppurating buboes to prevent rupture and thereby avoid chronic sinuses. Secondary bacterial infection will follow surely surgical drainage which often results in chronic extensive ulceration. Torpin and Dienst mention that "frequent intradermal tests," 0.1 c.c. vaccine, may prove valuable. If draining sinuses develop, frequent irrigation or possibly injection with mild cauterizing fluids or Menciere mixture may be used. Formalin, phenol and other caustic agents have fallen into discard.

GRANULOMA INGUINALE

Certain proponents claim that granuloma inguinale is an infection caused by Donovan bodies or bacilli while others feel that these uncultured organisms are not true bacteria, but possibly artifacts, and further suggest that a virus is the responsible agent. The disease is essentially a local process and extends by direct spread. Lesions are usually vulvar and inguinal, but may involve the anus, the vagina, the cervix and even extragenital organs.

The majority of reports fail to discuss any significance or importance of this clinical state in relation to pregnancy, labor or the puerperium. Its general infrequency destines only a rare occurrence with pregnancy. Yet this rarity does not pardon ignorance or neglect of such possibilities.

Torpin and Dienst[11] recommend Wright's stain for smears presumably containing Donovan bodies. Pund and Greenblatt[14] observed in tissue sections an affinity by the Donovan bacilli for silver salts. Hematoxylin and eosin have been used in biopsy material by some with fair success.

The lesion is usually elevated, meaty, reddish and somewhat resembles granulomatous tissue. It is a superficial skin lesion. It is hypertrophic in nature and may become secondarily infected, thus associated with putrid or other foul odors.

Antimony and potassium tartrate (tartar emetic) and also fouadin (fuadin) are specific therapeutic agents. Antimony potassium tartrate is dissolved in saline solution and given intravenously daily or on alternate days. The first dosage is 0.04 Gm. and is increased with each treatment by .01 Gm. until 0.1 Gm. is reached. The medication is continued until the patient is clinically cured except in the event of intolerance. Rheumatoid pains are the most likely symptom of intolerance. Prompt and immediate clinical response should be anticipated.

Williamson, Anderson, Kimbrough, and Dodson[15] endorse fouadin and prescribe it intramuscularly in 7 per cent solution, giving 1.5 c.c. the first day, 3.5 c.c. the second, 5 c.c. the third and 5 c.c. on alternate days for six more doses, or a total of 40 c.c. in fifteen days. It seems to cause less reaction, yet it is more costly than potassium and antimony tartrate.

Scarring may follow in the wake of the receding granulomatous tissue and conceivably might thereby predispose to dystocia. An unestablished argument has been advanced that the disease, especially when involving the vagina and cervix, should spread more rapidly during the gravid state because of the succulence and vascularity of the tissues.

Thus far reports do not reveal the transmission to the fetus in utero, but surely there is a fair possibility of contamination during birth. Accordingly such exposed babies need careful observation. Perhaps proper cleansing at birth and the application of a mild antiseptic as ammoniated mercury ointment to the delicate sensitive skin might offer some means of prophylaxis.

LYMPHOGRANULOMA VENEREUM

The virus disease lymphogranuloma venereum is found ordinarily in adults and rather rarely in pregnant patients. Although it usually manifests itself distinctly and often extensively locally, von Haam and D'Aunoy[16] point out that it is a systemic disease. Encephalitis is one of the remote infections as evidenced by the "symptoms of fever and headaches," and by recovery of the virus from the spinal fluid. The virus is transmitted by genital contact and seems to occur ordinarily in unhygienic and poor patients.

Characteristically in the female the lymphadenitis extends from the primary lesion, a papule, ulceration, or macule, which develops and vanishes, usually unnoticed by the patient, to the perirectal lymphatic structure. The femoral and inguinal glands are sometimes involved. Unless the inflammatory process is quite extensive the internal genitalia remain free. Accordingly, fertility on this basis remains unimpaired, and several observations confirm this conviction. Very excessive tissue reaction ends in complete obstruction of the rectum (necessitating colostomy) and often the elimination of all space in the pelvis by a firm inelastic inflammatory tissue. In extreme states necrosis may involve any of the pelvic structures, more likely the vagina, rectum, rectovaginal septum, ischiorectal fossa, and/or much of the lower pelvis.

After the reaction reaches a given point (varying extremely in patients) it remains stationary for an uncertain period, after which an involution, incomplete to a variable degree, follows. With sufficient involution some physiologic functions, such as normal bowel action, are reëstablished. After this a colostomy wound may be closed. Inasmuch as the Frei test remains positive for years after the original infection, it is necessary that the clinical findings confirm the diagnosis. The intradermal injection of 0.1 c.c. antigen (attenuated human pus or mouse brain) should produce a papule 7 mm. or more in diameter with a wider induration and hyperemia for a typical positive reaction.

Human source varies in its concentration; yet Binkley and Love[17] find it more reliable than mouse brain antigen. Grace and Suskind,[18] however, advocate mouse brain antigen. So far, it is the only available

commercial source and is uniform in its potency. When the mouse antigen is used, a control of non-infected mouse brain emulsion should be employed. Careful observations, after the twenty-fourth hour and up to the seventy-second hour will almost exclude false positive and false negative evaluations.

A specific and efficient agent would be a therapeutic boon. Perhaps more favorable response has occurred with the use of the Frei antigen of human source than other agents, unless sulfanilamide, now under investigation, should prove effective. The mouse antigen has not been used therapeutically. Human pus is diluted from 1 to 4 to 1 to 10 with saline solution and the virus killed by exposure to 60°C. temperature for two hours on two successive days. Torpin, Greenblatt, Pund and Sanderson[19] state that the intravenous route has not been shown to be more effective. The intravenous dosage starts with 0.05 c.c. and is increased gradually to 0.3 c.c. Intramuscular doses begin with 0.1 c.c. and increase to 2 c.c. This therapy is continued until the condition improves or fails to respond. Shropshear,[20] Knight and David,[21] Shaffer and Arnold,[22] Marino, Turell, Buda and Nerb[23] announce a moderate to a good improvement after sulfanilamide administration. In the absence of concrete data moderate amounts only of sulfanilamide should be tried until more information is available on the optimum dosage. Moreover, not all cases have been cured by this drug.

The few observations made during pregnancy indicate an unaltered effect upon the disease process. The disease may, on the other hand, alter appreciably the course of labor through dystocia from serious or impossible obstruction to the birth canal. Special managements have been used in some cases at the Provident Hospital (Chicago) because of pelvic obstruction (Wilson and Hesseltine[24]). The tragedies of Anderson,[25] Vignes,[26] and Gaines and McDowell[27] illustrate this point more emphatically. Fortunately, the combination of pregnancy and lymphogranuloma venereum is infrequent.

Sterility may result if there is injury to the uterine cavity, tubes, or ovaries, yet conception occurred in a patient after colostomy to relieve bowel obstruction.

Tests by Dich[28] and Babonneix, Fouraine and Lafont[29] revealed positive reactions in children. Yet of the entire group only one case report suggests congenital transmission. This baby had a positive Frei reaction on the fourteenth day of life, but it was without clinical manifestations.

Wilson and Hesseltine[24] found only one positive reaction in several children born of mothers with typical clinical lesions and typical reactions to intradermal Frei antigen.

All babies whose mothers have lymphogranuloma venereum should be observed and tested over a prolonged period for this disease.

GENERAL DISCUSSION AND CONCLUSION

Since extragenital lesions of the various venereal diseases have been reported and well proved, one may well anticipate such possibilities for the baby, due to inoculation as it traverses the infected birth canal. Syphilis may be acquired from a primary genital sore. Gonococci may find their way to a favorable nidus in the newly born child through contamination at birth. Certainly, chancroid, granuloma inguinale and lymphogranuloma venereum must present such risks at the natal period.

Gonorrhea is a major problem because of the possibility of spread to the maternal internal genitals and the peritoneal cavity in the postpartum period, and also because gonorrheal conjunctivitis in the infant occurs even in spite of prophylactic measures, not to mention the infrequent genital infections in the infant.

Syphilis is the scourge of the lot, for most pregnant women with this disease are without symptoms and usually without clinical findings. Every effort must be ventured to eradicate congenital syphilis. Although new mercurial, bismuth, and arsenical prepara-

tions are offered to the profession from time to time as more efficient and safer, their use during gestation must be postponed until enough investigation has been made to prove their value. Castello and his associates[30] and Goldberg[31] state that neoarsphenamine is the most dependable arsenical available from the viewpoint of the fetus. McCord uses mercury in place of bismuth as it is without pain and avoids frightening the patient by use of a needle.

The incidence of syphilis varies in different communities and in different groups of the same area. It is found in about 1 per cent of the Chicago Lying-in Hospital patients.

Every genital sore or lesion during pregnancy should be investigated. All discharges should be examined. Smears and cultures from the cervix and urethra are indicated if there is any question of infection of these regions. The smear should be stained by Gram's method (gentian violet followed by Gram's iodine, destained and then counterstained with safranine). Cultures are practical, but only in centers able to prepare fresh mediums and where the cultures may be immediately and properly incubated.

Every woman in every pregnancy should have a serologic (Wassermann, Kahn, or other) test at the first visit. Prevention of congenital syphilis is the only justifiable therapy. Patients must be "educated" to the value and benefit of adequate and intelligent prenatal care beginning in the first trimester. Every physician should make adequate serologic tests to exclude syphilis in every gravid patient in every pregnancy and treat actively each case of syphilis throughout the pregnancy if he is to practice the best obstetric medicine. This is rendering the best possible service to the mother and to the unborn child.

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While we still have destructive wars, famine and pestilence are not now the important factors in depopulation in most civilized countries. . . . The voluntary restriction of reproduction caused by the practice of contraception and the induction of abortion has much more effect on the equalization of birth and death rates than did the excessive mortality in the presence of unlimited propagation.
From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

RELATION OF TUBERCULOSIS TO OBSTETRICS

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SINCE tuberculosis is conceded to be a serious problem among girls and young women and since its incidence in this group is not diminishing as rapidly as in other age and sex groups of the general population, the association of tuberculosis and childbirth continues to be an important problem in preventive medicine. Edna E. Nicholson of the National Tuberculosis Association, in her study of tuberculosis among young women, states: "We know this phenomenon [i.e., the relative high death rate among girls and young women] has existed in the United States at least since 1900, and in view of the fact that mortality figures of England, Wales and Ireland show the same deviation as far back as 1860, it seems reasonable to suppose that for one reason or another, young women have always been more prone to die of tuberculosis than have their young brothers or older sisters."

Notwithstanding the tremendous amount of very excellent educational and preventive work accomplished during the past thirty years, tuberculosis is still responsible for some 60,000 deaths annually in the United States. Of this number about 29,000 are females and approximately 18,000 of these are between the ages of 15 and 45 years. Just what proportion of this latter group became pregnant and aborted or had premature labor or gave birth at term is not known. There are no available statistics with which to answer this question. We do know however that, as a general rule, the gravida who has tuberculosis does not receive adequate care during pregnancy, labor, the puerperium and for a sufficient period of time following these events properly to "cure" active tuberculosis or keep quiesent tuberculosis "arrested." Neither does she always receive adequate obstetric attention. We know also that one of the main reasons for this state of affairs has been the woeful lack of coöperation between accoucheur and phthisiologist, stimulated by the almost complete absence of proper hospital and sanatorium facilities. Thus we may well account for much of the confusion that exists as to the effect of pregnancy, parturition and the puerperium and their end-results upon tuberculosis.

For the past few years, however, this gap has been slowly "closing in" because medicine has gotten to a stage in its evolution where no sane physician believes himself competent to practice medicine without help from his colleagues who, although they may not be classed as specialists, have superior knowledge in one field or another. No modern obstetrician or physician doing obstetrics therefore should attempt to handle a case of pregnancy associated with tuberculosis without the diagnosis, advice and full coöperation of an internist with knowledge of tuberculosis, or better still a phthisiologist or tuberculosis specialist. Furthermore, in view of the more recent improvements in case finding technique, in diagnosis and treatment of tuberculosis and in the management of pregnancy (prenatal care), labor, delivery and the puerperium, we should "now and here" cease quoting the statements and statistics put out by perfectly sincere authors of ten to twenty years ago. Such statistics are obsolete and are a detriment to an up to date understanding of this most important problem.

In still further substantiation of these statements, regarding lack of interest, coöperation and facilities among interested

groups, Alice M. Hill* called attention to the appalling fact that only eighty-seven, or 21 per cent, of 413 out of a total of 463 (413) that admit or retain pregnant women and take care of them through delivery; 247 or 60 per cent of the 413 sanatoria

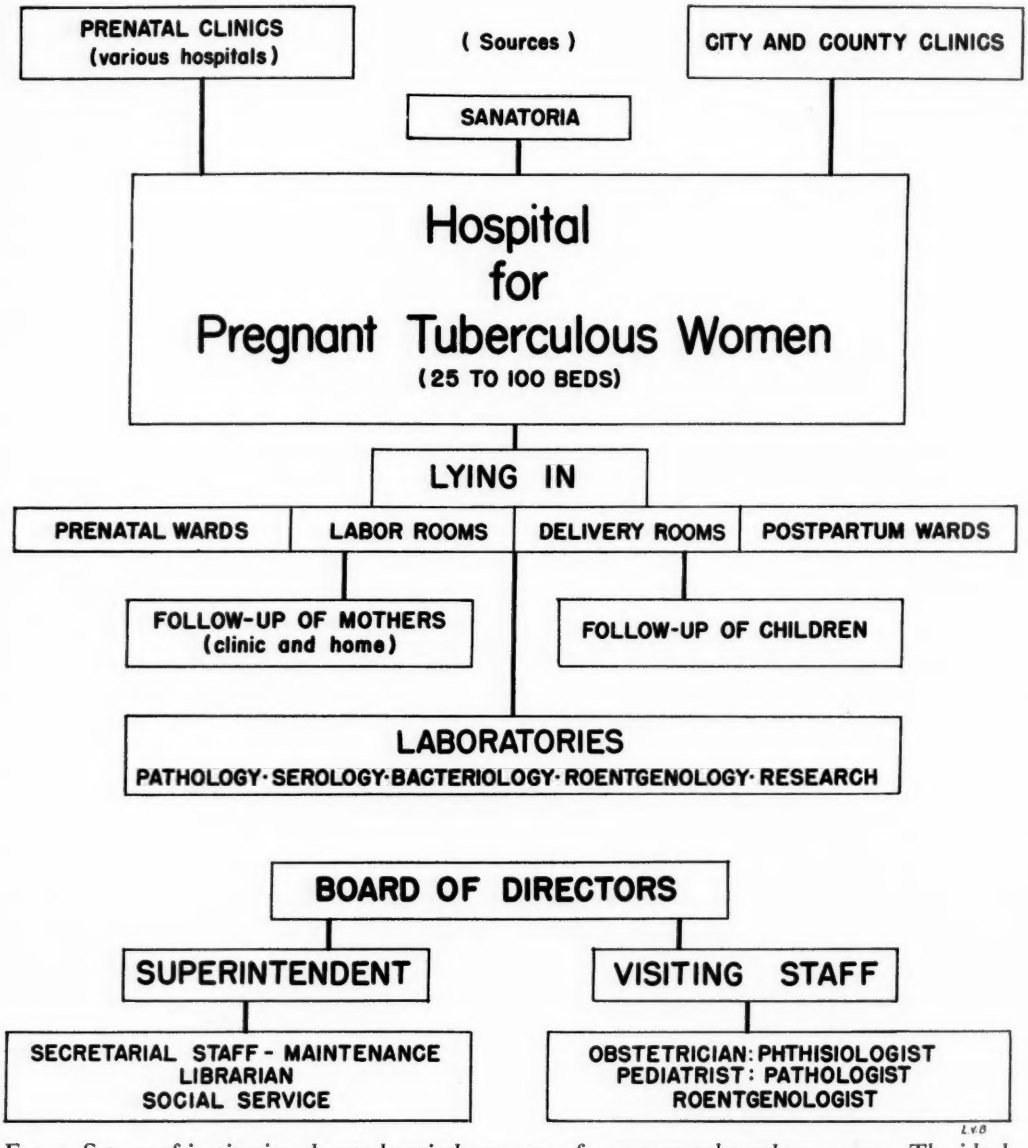

Fig. 1. Set-up of institution devoted entirely to care of pregnant tuberculous women. The ideal arrangement.

sanatoria in the United States, admit and retain pregnant tuberculous women and keep them through delivery. Of these institutions forty-three are general hospitals, thus leaving only forty-four tuberculosis sanatoria, or 10.6 per cent of the total admit pregnant women but transfer them to general or special hospitals or to their homes for the delivery. Furthermore, we find that 24 per cent of the private sanatoria do not admit pregnant women at all, and only 17 per cent of them keep the patient through delivery. Of the state sanatoria only 10 per cent keep their pregnant patients through delivery, while 71 per cent admit them before time for the

* While these figures were published in 1927 there is no reason to believe that conditions are materially different today. This is the unanimous opinion of two internationally known tuberculosis statisticians, who prefer to remain anonymous.

delivery. Of the county sanatoria 22 per cent keep them through delivery, and 65 per cent transfer them for delivery.

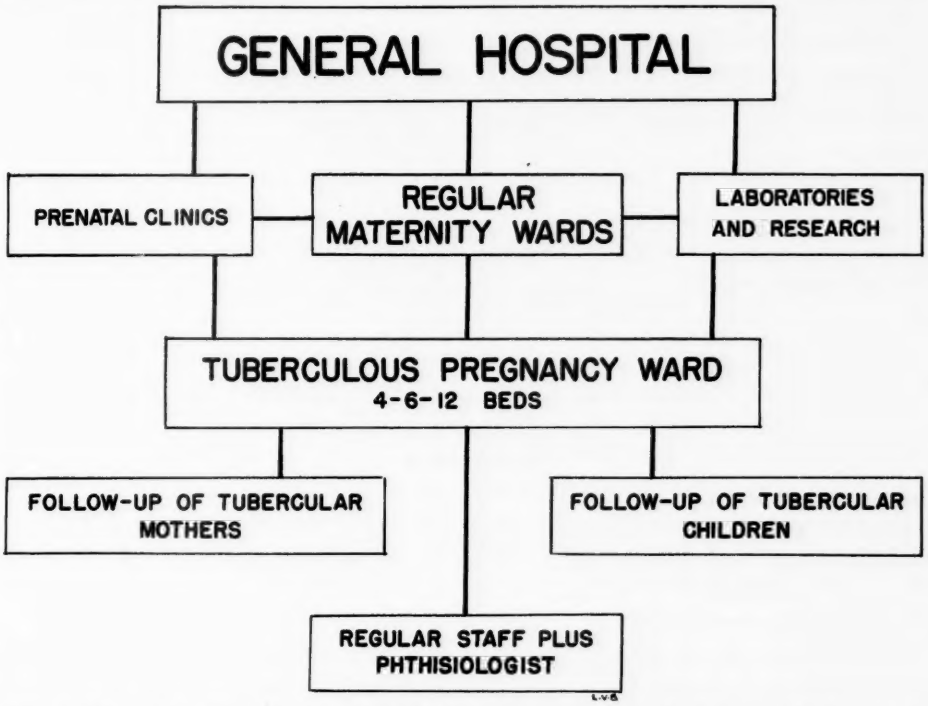

Fig. 2. Alternative arrangement of wards for pregnant tuberculous women in a general hospital.

In this report by Dr. Hill, nothing was said about the adequacy of the care these patients receive. Nevertheless, from the standpoint of their tuberculosis, there can be little doubt as to the adequacy of the treatment; from the standpoint of the pregnancy, labor and puerperium there is grave doubt. This is a natural supposition, for no one would expect an expert obstetrician interested in tuberculosis to be associated with a tuberculosis sanatorium, except perhaps those few situated in or near the larger cities. Conversely, it would not be expected that the phthisiologists of these institutions would be good obstetricians. Of the eighty-seven sanatoria reporting facilities for the care of pregnant tuberculous women, only a very few, probably not over ten to twelve, actually carried out the proper management of the pregnancy, the labor and the puerperium. The vast majority did the best they could with the facilities they possessed, realizing full well their inadequacies. The greater city of New York is not in much better position for there are only two or three institutions in the city where the tuberculous woman who is pregnant can be adequately cared for through delivery and beyond the lying-in period for as long as is necessary to render her safe to return home.

What then is to be done to insure adequate care, both medical and obstetric, for the pregnant tuberculous woman? The following plan is suggested:

1. The ideal set-up for the adequate management of tuberculosis and pregnancy would be a special institution devoted exclusively to the care and treatment of pregnant tuberculous women. Here would be working in close harmonious coöperation a specialist in tuberculosis; an expert obstetrician interested in tuberculosis; a pediatrician also interested in tuberculosis; a roentgenologist; and the whole group supported by good pathologic, serologic and bacteriologic laboratories. In such an institution the tuberculosis, the pregnancy, the labor and the puerperium and the baby immediately after birth, could be adequately handled, and the "follow-up"

of mother and baby could be ascertained with accuracy. Furthermore, research in pathology, serology and bacteriology of tuberculosis, including congenital tuberculosis, could be pursued to the end that something definite and constructive might supplant the confusion and chaos now existing.

2. In lieu of this ideal set-up the following is proposed, viz., that each hospital group interested be allocated a certain number of beds for pregnant women with tuberculosis and that these patients be under the direct supervision of a tuberculosis specialist in coöperation with an obstetric specialist who is interested in tuberculosis. After the seventh month of the pregnancy the obstetrician should assume first control of the patient with the tuberculosis specialist coöperating, the obstetrician to continue in charge until after the postpartum period (two or three weeks or longer), following which the tuberculosis specialist again assumes charge and manages the case as he would any other case of tuberculosis.

The management of the baby should be put under the direct supervision of a pediatrician interested in tuberculosis as soon as the umbilical cord is ligated. Decision as to the extent of mother-baby association, if any, can thus be made before contact infection of the baby takes place. This arrangement is of the utmost importance, particularly where the mother's sputum is positive for tubercle bacilli. The pediatrician, of course, should follow the child through the adolescent period and see to it that a good internist interested in tuberculosis takes charge when he shall have finished his job.

With either of these arrangements (of course the first is the most ideal) research could be carried on by the various individuals concerned in the management of these cases and, with the coöperative teamwork of the various laboratories, reliable end-results could be ascertained. Moreover, classification, typing, diagnosis and management of the tuberculosis would become much more standardized than has hitherto been possible. Naturally, no plan will be successful unless the coöperating physicians—tuberculosis specialist, obstetrician, pediatrician, roentgenologist, pathologist, serologist and bacteriologist—are vitally interested in this type of work. For smaller communities where such complete coöperation is not possible, every effort should be made to obtain the services of one who knows tuberculosis. This is one situation where the various State Departments of Health or, in those states unable to coöperate, the United States Public Health Service, could render a valuable consultation service without in any way encroaching upon the rights and privileges of the private physician. Since the President has proposed a plan for government constructed hospitals in communities where there is need but not the finances, some of this construction could be carried out to provide improved facilities for the care of pregnant women who have tuberculosis. No better way of spending public funds, it seems to me, could possibly be found.

EFFECTS OF PREGNANCY ON TUBERCULOSIS

At the outset of any discussion of the effects of pregnancy upon tuberculosis we should have clear in the "mind's eye" that it is not pregnancy alone that is meant but the entire cycle of events implicated in childbirth—gestation, labor, delivery and the puerperium.

It should be constantly kept in mind that the type or character of the tuberculous lesion is far more important than the extent of the disease. Merely the designation of whether a given lesion is minimal, moderately advanced, or far advanced is not nearly so important, although, of course, it is quite necessary, as the pathologic character of the lesion. Experience, during the past decade has impressed upon the phthisiologist the fact that in the exudative or pneumonic types of the disease the prognosis is not nearly so favorable as in the productive or fibrous types. This knowledge becomes of more value in

relation to tuberculosis and pregnancy when we bear in mind that the more destructive and fatal types of tuberculosis (exudative or pneumonic) occur more frequently in the younger age and sex groups, particularly in young females, whereas the less destructive types (productive or fibrous) occur more frequently in those past middle life. In other words, during the most prolific reproductive period of a woman's life, she is also subject to the most devastating types of tuberculosis. Is it any wonder therefore, that before the advent of a more thorough understanding of the tuberculous process and a better coöperation between the modern phthisiologist and obstetrician, the maternal mortality rate in pregnancy, parturition and the puerperium in tuberculosis remained alarmingly high? Likewise, is it any wonder that abortion was so frequently performed?

Today the picture has changed. With the newer concepts of the pathologic type or character and clinical behavior of tuberculosis, the phthisiologists have developed improved methods of case finding, of diagnosis and of treatment. Some types require more heroic treatment than others. Whereas all types require the accepted routine "cure" treatment, including pneumothorax in a large percentage of cases, others require, in addition, the more drastic procedures of phrenicotomy or thoracoplasty, Incidentally, thoracoplasty, although requiring at least two extensive surgical operations, is not looked upon today as the mutilating procedure of doubtful value that it was a decade or more ago. Its results are indeed gratifying. Surgery has come to be another important affiliate in the treatment of tuberculosis.

Now let us ask the question—What changes, if any, in the treatment of the tuberculosis are indicated during pregnancy, labor and the puerperium? Formerly this was a much debated question; today it is certain that the pregnant woman should have identically the same treatment as her nonpregnant sister who has tuberculosis. In more recent years, collapse therapy has been practiced extensively during pregnancy with gratifying results for the tuberculosis and apparently with no ill effects on the gestation, the labor, or the delivery. There are several reports in the recent literature on this phase of the subject. For example, Seely, Siddall and Balzer of Detroit, report in detail a study of fifty-four cases of tuberculosis and pregnancy treated with collapse therapy before and during the pregnancy, immediately after labor and during the puerperium, with uniformly good results. They had nineteen cases in which treatment was begun *before* pregnancy and 90 per cent of these were arrested or improved. In thirty-five cases treated during pregnancy, 77 per cent showed arrest or improvement, while 23 per cent were made worse and of this latter group fourteen per cent died within one year after confinement.

In a more recent report the same authors cite ten cases of pregnancy and parturition following thoracoplasty for advanced tuberculosis from the Herman Keifer Hospital of Detroit. They were also able to find twenty-one cases in the literature, making a total of thirty-one such cases for study. In this group, interestingly enough, four successful thoracoplasties were done during pregnancy. These thirty-one women gave birth to thirty-four babies, five prematurely. "One mother died and five others had serious exacerbation of the tuberculosis during pregnancy or within one year after delivery." Thus 19.3 per cent of these mothers had a reactivation of their tuberculosis, one to the extent that she died, while 80.7 per cent were not affected or at least not made worse.

Another report by Ornstein and Epstein from Sea View Hospital in New York, cites a group of eighty-two pregnant women with tuberculosis whom they delivered, in which 24.3 per cent were made worse. Of these 12.2 per cent died, thus leaving 75.7 per cent in the "stationary" or improved group. In this series there were twelve women upon whom thoracoplasty had been performed and who later became pregnant,

delivered their babies (one of these women had two children) and "not a single one of them had any appreciable reactivation of tuberculosis." Thus two geographically widely separated groups of tuberculous pregnant women, under almost ideal supervision, show comparable excellent results. When it is recalled that patients on whom thoracoplasty has been performed are far advanced cases with cavitation these reports appear little short of witchcraft to those who maintained that no woman with far advanced active or inactive tuberculosis, regardless of the type of lesion, should have a baby. Those familiar with the statistics on tuberculosis and pregnancy will see at a glance that the modern figures quoted above and obtained by coöperative teamwork, with adequate facilities, are many times better than those of ten and twenty years ago. Thus again we reiterate that the older statistics are obsolete.

It seems evident from a review of the recent literature coupled with a limited experience, that while collapse therapy is the greatest advance in treatment for the pregnant tuberculous woman to date, it does not entirely solve the problem. It still cannot be said with propriety, as some recent observers have stated, that pregnancy *has no effect* on tuberculosis. We can say, with certainty, that it does, but that with the more heroic methods in the treatment of the tuberculosis, coupled with improvement in obstetric care, and closer and more harmonious coöperation between the patient, the accoucheur and the phthisiologist, the entire problem is certainly less difficult at the present time than it has been in the past.

EFFECT OF TUBERCULOSIS ON PREGNANCY

The effect of tuberculosis *per se* on the course of gestation is negligible. It has no effect on fecundity; in fact in many instances where the tuberculosis is not debilitating and the "cure" is conscientiously taken, fertility seems to increase as the general health improves. The development of the fetus is normal. Abortion or premature labor is somewhat more frequent than in the nontuberculous patient, particularly, in those cases with exhausting cough, hemoptysis, fever and marked general debility.

In the less advanced cases going to term or near term the labor may be completed without cause for alarm. In the far advanced cases labor may be tedious, prolonged and fraught with many dangers to the mother, as for example in the presence of dyspnea, cough, hemoptysis, impending cardiac failure, pulmonary edema or spontaneous pneumothorax.

Upon the puerperium, minimal or moderately advanced tuberculosis seems to have no effect; the incidence of postpartum hemorrhage is no greater and involution is generally not retarded. In the more active, extensive and progressive cases there is apt to be excessive hemorrhage and involution may be tardy.

From the accumulated evidence to date, it may be concluded that whatever deleterious influences tuberculosis has on pregnancy, parturition and the puerperium are not due to the tuberculosis *per se* but are entirely dependent upon the general status of the woman, i.e., whether she was debilitated or in good physical condition before conception, during gestation and following parturition.

Pregnancy complicating laryngeal tuberculosis is distinctly bad. According to Myerson, the incidence in females in the age group 15 to 40 years runs about parallel with that for pulmonary tuberculosis in this age group. Age is a definite influencing factor in tuberculosis of the larynx. The older the patient the less likelihood of her developing laryngeal tuberculosis. Again, therefore, we see the young woman a possible victim of a grave complicating tuberculous lesion, superimposed upon her already far advanced pulmonary tuberculosis, in the presence of pregnancy and confronted with the possible deleterious effects of labor and the puerperium. Truly a gloomy picture! We can readily agree

with Myerson and others, that pregnancy should not be contemplated in the presence of laryngeal tuberculosis.

While congenital tuberculosis is possible, as shown by Whitman and Green who have collected from the literature forty-seven authentic cases, it is relatively rare. Although constantly on the lookout, I have never seen a case, but believe if systematic study was made on every baby and placenta of a tuberculous mother, particularly in the more advanced cases, and especially the acute miliary type, more cases of congenital tuberculosis would be found than have hitherto been discovered. Furthermore, "Sitzenfrey has demonstrated in women dying of tuberculosis the presence of bacilli in the interior of ova while still within the Graafian follicles" (Williams). This could lead, although impossible to prove, to congenital tuberculosis.

MANAGEMENT OF PREGNANCY AND TUBERCULOSIS

The active management of pregnancy complicated by tuberculosis naturally divides itself into (1) the general and (2) the obstetric.

The general treatment of the tuberculosis is, as stated above, identical with that for the nonpregnant patient. With, however, the added "load" of pregnancy, causing an increase in metabolism, oxidation, and innervation, which in turn throws extra work upon the circulation and elimination, more intensified attention to fresh air, diet, rest and exercise must be given. Otherwise the phthisiologist, in full coöperation with the obstetrician, manages the case as he would any other patient with tuberculosis. Likewise, the obstetrician manages the pregnancy, the labor and the puerperium just as he would an obstetric patient who had any serious systemic disease. Adequate prenatal care*—never omitting a single item that the most meticulous authorities have laid down as adequate—must be given the gravida who has tuberculosis. If "a watchful eye can save a life when diligently and constantly focused on the object of its stare" in obstetrics or tuberculosis alone, think how very much more indispensable this becomes in the combination of pregnancy, parturition, the puerperium and tuberculosis. Intelligent, friendly and full coöperation between patient, phthisiologist and accoucheur is required if the best results are to be obtained.

The obstetric management includes (1) the question of the interruption of the pregnancy; (2) the method by which interruption is best accomplished; and (3) the best method of delivery at or near full term.

As to the question of the interruption of the pregnancy there are two valid indications: (1) the vital indication, where it is necessary to save the life of the gravida with far advanced tuberculosis who in the opinion of the phthisiologist is in immediate danger of dying; and (2) the prophylactic indication, where abortion is done after all therapeutic measures have failed to retard the progressive extension of the disease, which may be expected to be still further activated from pregnancy, labor and the puerperium. The vital indication is rarely, if ever, indicated. Today such a patient would not be allowed to become pregnant, and if by chance pregnancy did take place, interruption of the gestation would probably *not be recommended.* Abortion would be equally, if not more, hazardous than labor at or near full term, and in addition would provide no handicap to the offspring. The prophylactic indication is definitely on the wane. With the newer concepts of the pathologic and clinical behavior of the various types of lung tuberculosis and the more heroic methods in their treatment, as outlined above, therapeutic abortion is not practiced to the extent that it was in former years. This is as it should be, for as in heart disease, thyrotoxicosis, diabetes and affections of the kidneys, etc., the more accurate our knowledge has become the better we understand these serious systemic diseases

* The reader is referred to any standard text for details on prenatal care.

and the better we are able to cope with them in the presence of pregnancy and parturition. What was formerly an indication for therapeutic abortion is not an indication today. This is particularly true of tuberculosis and pregnancy. Consequently therapeutic abortion is not considered necessary except where the tuberculosis cannot, for various reasons, be properly managed; when the tuberculous lesion is so far advanced as to preclude successful "arrest" when first seen by the obstetrician; or in the very fulminating malignant types of caseous pneumonic tuberculosis with cavitation that do not yield to collapse therapy, including thoracoplasty.

The method of choice in interrupting the pregnancy and the conduct of labor at or near term constitutes a very important phase in a pregnancy complicated by pulmonary tuberculosis. First of all, the best method whether early or late, is that method which will cause the *least trauma and shock* to the mother. Interruption during the first six to ten weeks can oftentimes be done by the use of the cervical and vaginal pack, particularly in the multiparous patient, followed by curettage under local, cyclopropane or gas-oxygen anesthesia, or in suitable cases, under obstetric analgesia without anesthesia. If the cervix is long, firm, and tightly closed, anterior vaginal hysterotomy under local, spinal, sacral, or cyclopropane or gas-oxygen anesthesia is the operation of choice. We usually induce obstetric analgesia by some one of the many methods—morphine-scopolamine, nembutal, sodium amytal, paraldehyde, etc.—before administration of the anesthesia (local or general). This proves very satisfactory for both patient and operator. We *never* use ether anesthesia unless there is no other way out. From the twelfth to sixteenth weeks, anterior hysterotomy following the above technique is the best procedure, except in those cases where the cervix is short, soft and patulous. Then rupture of the membranes, insertion of a vaginal or cervicovaginal pack or a Voorhees bag, or both, serves to start uterine contractions, to promote cervical dilatation and hasten uterine evacuation. Bleeding, should it occur, must be promptly controlled and shock vigorously combated. Remember that these patients are apt to be quite ill and debilitated, and hence succumb more quickly to trauma, hemorrhage, shock and sepsis than the average obstetric patient. Prevent trauma, conserve blood (De Lee) and prevent or promptly combat shock should be the motto of every obstetrician and gynecologist.

From the sixteenth to twenty-eighth week of gestation, artificial interruption should very rarely be undertaken, except in the very desperate cases where, in spite of proper treatment, the patient is rapidly growing worse. If intervention is decided upon, sufficient Roentgen ray (2000–3000 R) to cause abortion is given, or radium is inserted in doses of from 1200 to 1500 mg. hours within the pregnant uterus, using local or cyclopropane anesthesia. These doses of *x*-irradiation are not usually sufficient for the production of permanent castration, but do bring on an amenorrhea of from a few months to two or more years. Vaginal hysterotomy is a very efficient, quick, and easy method of evacuation of the uterus and the method we prefer unless the patient is extremely ill. In the latter case *x*-ray is preferable. Following the vaginal hysterotomy, when the patient has improved, sterilization, if advisable, can be accomplished by *x*-ray or radium. In young women where it is not deemed advisable to use *x*-irradiation, the oviducts can be ligated per vaginam if the patient's condition warrants at the time hysterotomy is performed, or if, as some operators prefer, abdominal hysterotomy is performed, the Fallopian tubes can be ligated very easily. Should every patient aborted be sterilized? Certainly not, for with proper medical care, it might well be possible for the tuberculosis to become "arrested" and after two or three years or more the patient could again become pregnant and, under proper care, carry to or near full term with safety.

From the twenty-eighth to fortieth week, nothing can be done that will improve conditions. The phthisiologist having gone the limit in treating the tuberculosis, watchful waiting may seem cowardly, but operative interference is almost sure to terminate fatally. However, here as elsewhere in medicine and surgery, individualization counts for a great deal. Under certain extenuating circumstances almost any established form of treatment may be altered, oftentimes with fairly good success.

If the pregnancy has been carried to or near full term the labor should be made as easy and short as possible. When labor pains are at regular and frequent intervals and the cervix is dilated to the size of a fifty-cent piece, (2 to 3 cm.) morphine-scopolamine analgesia, or some one of the many other effective and well known methods of securing obstetric analgesia, should be employed to a degree sufficient for the relief of the stress and strain of the labor. As soon as the cervix is fully dilated, rupture of the membranes, if these have not previously ruptured, episiotomy and the application of forceps and immediate delivery, using *local*, gas-oxygen or cyclopropane anesthesia during the active delivery, is the procedure of choice.

If the breech is presenting, follow the same routine, except complete the delivery of the breech as soon as possible. *Full cervical dilatation* should be present before any method of delivery is carried out. In the presence of a normal pelvis and baby, with fully dilated cervix and ruptured membranes, pituitrin, ¼ to ½ c.c., may be given. This with episiotomy and gas-oxygen anesthesia, will accomplish delivery in the shortest possible time and with the least shock to the mother. Piper forceps applied to the after-coming head in these breech deliveries often saves time and trauma, both to baby and mother.

Version and breech extraction should not be performed in the presence of advanced tuberculosis, except on strictest indications, because of the deep anesthesia required, the extra trauma that is necessarily produced and the greater chances of infection. This is particularly true in the collapse therapy cases. The obstetrician must plan the method of delivery, having obtained accurate pelvic measurements (by *x*-ray if possible) and estimated the size of the baby, so that version and extraction or other "shocking" operative procedures will not, as a last resort, have to be undertaken. We believe, when there is any doubt, either of the ability of the pulmonary lesion to withstand the strain of labor in a given case or where the bony pelvis and/or the child shows evidence of possibly causing dystocia, elective cesarean section or cesarean section after a short test of labor without progress is indicated.

If there is disproportion between the child and the pelvis or other cause for apprehension on the part of the obstetrician as to the outcome of the labor, elective cesarean section, at or near term, under *local* or gas-oxygen or cyclopropane anesthesia, should be done. We use *local* in the form of abdominal "block" and find it highly satisfactory. We do not use spinal in these patients. In cases where collapse therapy has been practiced, particularly thoracoplasty, we believe cesarean section, using *local* block anesthesia, should be more frequently employed. Certainly in the primipara this procedure would obviate the relatively long first stage and prevent the respiratory embarrassment that comes with strong second stage pains in the patient who has only one, or perhaps less than one useful lung. Furthermore, cesarean section is the method of choice when cardiac or nephritic lesions, excluding, of course, eclampsia, complicate the pulmonary status. It goes without saying that if cesarean section is to be the method of choice it should be performed by a competent operator in a well equipped operating room. Vaginal cesarean section should *never* be done after the seventh month of gestation, because even in expert hands, the trauma and blood loss associated with this operation are considerable. This not infrequently causes an extreme degree of

shock which in turn is distinctly injurious to the tuberculous patient, especially in the advanced exudative and pneumonic forms of the disease.

These patients must be protected against long, tedious, exhausting labors and difficult, traumatic, or operative deliveries, performed late in labor when the more conservative plan of delivery has failed. Here, as elsewhere in clinical medicine, conservatism may turn out to be radicalism when not tempered with good judgment. To make labor as comfortable and non-exhausting, and delivery as easy, short and nontraumatic as possible, is a good working rule. These facts cannot be too strongly emphasized and I dwell upon them because I believe the accoucheur—general practitioner and specialist—has had to take the blame far too frequently for the reactivation of a healed tuberculous lesion or the spread of an active one that the phthisiologist had under control. Furthermore, it must be constantly kept in mind by the accoucheur that hemorrhage and shock should be prevented as far as it is possible to do so and that when they occur, prompt and vigorous treatment is urgently indicated. Transfusion should be given without delay, or without regard for the tuberculosis, and in sufficient quantity to replace the blood loss. Shock cannot be successfully combated until the blood vessels have their fluid loss (plasma) restored. Prevention of hemorrhage and shock or shock without hemorrhage is the working axiom in this connection. Remember, in every obstetric procedure, Dr. De Lee's oft repeated slogan "conserve blood."

MANAGEMENT OF THE PUERPERIUM

The obstetric management of the tuberculous patient during the puerperium is essentially the same as for any other patient. The phthisiologist accepts full responsibility for the tuberculosis. In the milder healed lesions nothing need be done except repeated check-up of the tuberculosis and "watchful waiting" to be sure reactivation has not taken place. In cases where collapse therapy has been practiced prior to and during pregnancy it should be carried out during the puerperium for as long as indicated. There may be cases where collapse therapy is indicated for the first time immediately after delivery. In other cases only some form of abdominal compression as obtained with the diaphragm lift which elevates and restricts the movements of the diaphragm may be necessary. We have used the Burgess Gordon type of abdominal compression binder with satisfactory results. It can be used in all cases—non-collapsed and collapsed—immediately following delivery and for as long as indicated.

Excessive postpartum bleeding is not uncommon in the tuberculous parturient. Matthews and Bryant in 317 ex-Trudeau patients reported a 13 per cent incidence of postpartum hemorrhage, whereas the incidence for the general population is 2 per cent. These data, however, were obtained from the patients, not the doctors who delivered them, and may be subject to inaccuracies. Nevertheless, other writers have reported a definitely increased incidence in postpartum hemorrhage of greater or less severity, particularly in advanced tuberculosis where the patient is in poor general condition. Consequently this accident must always be kept in mind. Prompt and appropriate treatment for the control of excess bleeding, including blood transfusion is the proper procedure. Furthermore, the accompanying shock must be promptly combated by morphine, application of heat to the entire body, hypertonic intravenous dextrose (300 c.c. of 25 per cent solution) followed by blood transfusion. Delay in these procedures may well mean the difference between life and death in the mother who has advanced tuberculosis. With the modern methods of handling the tuberculosis, the pregnancy, the labor and the delivery, the puerperium *per se* does not present the hazards that it formerly did, provided, of course, these methods are available. Furthermore, it is more generally recognized today that

proper care must be given the tuberculous mother following the postpartum period for a sufficient length of time to make it safe for her to return home. The puerperium is often a critical period for the non-tuberculous parturient and in the presence of tuberculosis the most careful supervision is definitely indicated.

LACTATION

Of the many questions relating to the effects of pregnancy and parturition on tuberculosis, nursing is one phase that should demand most careful consideration. The baby should never be allowed to nurse, except perhaps in those cases where the mother has a minimal or moderately advanced healed lesion with a negative sputum. If she is in good general condition and it is highly desirable to give the baby a good start in life, lactation may be permissible. In such cases the baby may be nursed from six to eight weeks *only*. All others should *absolutely not* be nursed. The objections to nursing are, of course, the danger of infecting the child and the added drain upon the mother's strength. The possible ill effects on the recently delivered tuberculous mother of the extra work and worry of the household, particularly under strained economic conditions, are perfectly evident to the practical clinician. A "breakdown" in the mother may just as well be due to child-rearing as to child-bearing. Nowadays, fortunately for these mothers, weaning the baby is not the serious problem that it was in former years. The pediatricians are more expert in feeding babies artificially, and are no longer skeptical regarding their survival, future development and longevity. Many reports substantiate this point of view. For example, Matthews and Bryant showed that out of 579 children 556 were alive fifteen years or more after birth, and 501 (86.5 per cent) of these were in good health; fifty-five (9.5 per cent) were below par in health and in only nine cases of tuberculosis were found or suspected. Barnes and Barnes state that 81 per cent of children born of tuberculous mothers are healthy and develop normally. Blisnjanskaja found that of 23,000 children taken from their tuberculous mothers and sent to the country, only seven developed tuberculosis (Jameson).

WHEN SHALL THE TUBERCULOUS PATIENT CONTEMPLATE PREGNANCY?

Another very important question that inevitably presents itself for consideration is: How long after "arrest" of the tuberculosis should a patient wait before assuming the responsibilities of pregnancy, labor and the puerperium? This will vary, of course, because of the multiplicity of factors concerned. However, it can be said that with the average run of tuberculous patients, from two to five years should elapse before pregnancy is contemplated. Generally speaking, in minimal or moderately advanced cases with the productive or fibrous type of lesion, from one to two or more years should be allowed, whereas with the exudative or pneumonic types three to four or more years may be necessary. Naturally, in the far advanced cases still more time, four to five or more years will be required. There will be patients who should never become pregnant because of the undue risk involved, while, on the other hand, there will be patients who will have several children. In fact we have seen several such women who have experienced no appreciable harm to their tuberculosis. This question, in its final analysis, must be decided by the coöperating phthisiologist and accoucheur after a thorough consideration of the pathologic lesion in each individual case, not overlooking the temperament, desires, wishes and willingness to coöperate of the patient herself. In other words, individualization of each case based on its own merits, as elsewhere in medicine, is the best and safest criterion upon which to base prognosis.

STERILIZATION

The question of sterilization of the tuberculous woman—nullipara or multipara—is important, first from the view-

point of the mental effect on the patient herself and secondly from the standpoint of the tuberculosis. There is always present the likelihood of complete "arrest" of the tuberculosis, in which case we are fairly sure that after an interval of two or three or four or more years pregnancy and parturition can take place without undue risk. For the woman who already has her family, however, the indication is clear; we have only to decide upon the method.

It is, of course, common knowledge that when women menstruate, no matter what else may plague them, they seem more content with their lot in life. Therefore, we believe castration by means of the *x*-ray or radium irradiation is contraindicated except in those in whom menstruation is slowing up to an unreasonable degree the recovery from their tuberculosis. In a number of young women in whom the slowing up process has been pronounced, I have advised temporary castration (a few months to two years or longer) with *x*-ray or radium irradiation and with very satisfactory results. One such patient later became pregnant, carried to term, and was delivered of a normal child without any apparent effects on the tuberculosis. Where simple tubal ligation is performed to prevent conception there is not the same disturbing element, since menstruation is not interfered with.

Contraceptives, of course, are employed and with good success, depending on the physician's advice, his knowledge of technique and the ability of the patient to coöperate. However, fear of pregnancy and the difficulty of getting multiple abortions performed, makes this form of birth control unpopular with a great many tuberculous patients. Those who have far advanced tuberculous lesions and do not wish to become pregnant or have been advised not to become pregnant had best be sterilized by whatever method seems most suitable.

SUMMARY

Every woman cherishes the hope of motherhood. The desire to reproduce is instinctive. She should therefore not be deprived of this hope unless there is no alternative. Sweeping statements cannot, with sincerity and honesty, be made regarding pregnancy in tuberculous women. We have no right to say "no woman with tuberculosis should bear children" nor can we say "pregnancy, labor and the puerperium have no influence on the course of tuberculosis." There is, however, "a middle of the road" attitude that can be assumed and with a reasonably thorough understanding of both the associated conditions we may look forward to the successful outcome in a large proportion of cases. Success, however, will very largely depend upon the status (active or inactive), the type or character and extent of the tuberculous lesion; the *economic status* and *the attitude* of the patient; the thoroughness with which the phthisiologist can control the lesion; the completeness of prenatal care and the adequacy with which the obstetrician manages the delivery and the puerperium. Without the complete coöperation of all concerned, particularly the phthisiologist who understands the pregnancy but disregards it and the obstetrician who is interested in tuberculosis, but sticks to obstetrics, the prognosis will remain uncertain. On the other hand, with full coöperation, along with the modern methods of case finding, diagnosis and treatment of tuberculosis and the improvement in obstetric care that is now generally recognized, the problem of the relation of tuberculosis to obstetrics will not be so troublesome and uncertain as in the past.

This relationship will not show satisfactory results, however, until better provision is made in every community for the proper care of the pregnant woman who has tuberculosis. Under the present set-up, case finding efforts, expert diagnosis and adequate management can only be carried out in the favored communities that possess the proper facilities and personnel. Surely it is not humane to continue to care for the pregnant tuberculous patient in the desultory and inadequate manner that

many of us have had to employ in the past. We need a keener appreciation of the facts by the general public; by those in control of hospitals and sanatoria; and, most of all, by the medical profession.

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CARDIAC DISEASE IN OBSTETRICS

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DISEASE in a pregnant woman is not the same in its course and results as in the non-pregnant patient. Though the name of the disorder may be the same, the coincidence introduces new and variable factors which drastically alter the manifestations and the diagnostic, prognostic and therapeutic problems. Gestation brings about physiologic changes in the prospective mother which may, and often do, change her vulnerability to certain diseases and also modify the homostatic reactions and compensatory phenomena. Certain pathologic conditions may arise which are peculiar to, and definitely associated with, the pregnant state. Furthermore, in obstetric medicine the problems of the attending physician are made more complex by the fact that two lives are involved. A dual viewpoint is essential if the full significance of these important and frequent problems is to be grasped. The obstetrician views the cases as those of pregnancy complicated by some coincident disease, whereas the internist inevitably reasons that these are cases of disease complicated by pregnancy. Either viewpoint alone is inadequate, for both are correct, yet individually incomplete. On the one hand the question arises as to what effect does or will pregnancy have upon the course of the disease, and on the other its corollary exists: what effect will the disease have upon the gestation and/or the products thereof? The answers to these pertinent questions and the application of such knowledge will vary with each and every one of the innumerable possible complicating coincidences. For example, it is well known that an active syphilis in a pregnant woman will cause serious or even fatal damage to the fetus, though the course of the maternal syphilis shows little change. In contrast, an active maternal tuberculosis rarely affects the fetus, but the pregnant state may lead to disastrous activation and exacerbation of the maternal infection. Thus the vexing question often arises as to the advisability of prematurely terminating pregnancy in order to safeguard the life or health of the mother. These decisions, as those involving the prevention of pregnancy, include social, legal, ethical or religious and psychologic questions as well as the more purely biologic or medical ones.

Many of the problems of obstetric medicine[1] arise prior to conception and the pregnant state; others arise during gestation, either coincidentally or with some etiologic association between pregnancy and the disease in question. In the former group of disorders it is often possible to foretell of later difficulties; frequently disaster is predictable if there is sufficient clinical acumen and judgment to evaluate correctly the significance of certain preconceptional disturbances. Disease arising during pregnancy is predictable less frequently, but it must never be forgotten that pregnancy per se confers no immunity upon the prospective mother; her vulnerability to disease is more often increased than decreased or unaltered.

Premarital or preconceptional health evaluation has become increasingly frequent and definitely more thorough, a definite advantage, for certainly there are few places in clinical medicine where forewarning is more valuable than in the practice of obstetrics. Public consciousness is awakening to the importance of such prophylactic health examinations, but the understanding is incomplete and unnecessarily limited. The obligation to foster and enhance the public's appreciation of thorough periodic health evaluation falls upon every practitioner of medicine. Certain

examinations are expected by the better informed patients; other equally important aspects are completely ignored because of perfectly natural ignorance. Such ignorance, however, is inexcusable in the physician. Serologic examination for syphilis is becoming a routine procedure before marriage; in many states it has been made obligatory by law. Search for evidences of heart disease is anticipated by the majority of young women requesting a preconceptional or premarital examination. On the other hand, many physicians and almost all patients are satisfied with a very superficial examination of the urine as evidence of adequate renal function. Such evidence is wholly inadequate[1,2] and, consequently, severe and dangerous renal disease is more frequently an unexpected problem in obstetric practice than cardiac disease. Both the heart and the kidneys are subjected to greatly increased physiologic burdens by pregnancy and it is only logical that the functional capacity of both structures should be carefully evaluated *before* these strains are imposed.[3]

Health inventory requires clinical skill, judgment and thorough, painstaking diagnostic study. In the acutely ill patient symptoms and signs are usually obvious and diagnosis is largely a question of elimination of the less probable explanations for the clinical picture, and proof that the chosen reason (diagnosis) is the correct one. Effective evaluation of the health and functional reserve capacity of an apparently well individual requires the discovery of obscure hints and occult evidences of early impairments, and the detection of suggestions of potential disease. Perfect physical fitness is exceptional. Although the great majority of abnormalities discovered by health evaluation studies are inconsequential, in preconceptional clinical examination they must be appraised with due consideration of the particular physiologic stresses imposed by the anticipated pregnancy. With such considerations in mind it is obvious that many findings may assume significance which ordinarily would be wholly immaterial. To do this well does not require any very special training, but it does involve conscientious thoroughness, time, and an understanding of the physiologic changes occurring in pregnancy.[1]

Unfortunately, many physicians consider health examination and physical examination as synonymous. The physical examination is but a part of the clinical study which constitutes a proper health evaluation. Of almost equal importance is the elicitation of the history of the patient and the intelligent appraisal of the data revealed. The history of past illness frequently reveals disease potentialities. For example, pyelitis in the past may be a forewarning of impending recurrence; a history of severe migraine with frequent bouts of debilitating nausea and vomiting may herald excessive vomiting in the first trimester of pregnancy. Likewise, evidence of rheumatoid phenomena in childhood should incite an especially careful search for evidences of rheumatic carditis and/or latent chorea. Such information is rarely volunteered by the patient; it must be extracted by prolonged and meticulously specific inquiry. The value of the history of the apparently well patient who is requesting a preconceptional prognostic opinion is not limited to the data regarding previous sickness: the psychologic and socio-economic background and the habits of the individual are of great importance, particularly when some organic defect may require prolonged limitation of activities or special care. In perplexing cases, where one is in doubt as to the advisability of the patient's attempting pregnancy but hesitates to deny a woman her priceless privilege of motherhood, the socio-economic status may be the deciding factor. Whereas one patient has the means, the patience and the character to follow rigid and prolonged restrictions of physical activities, another may be temperamentally or economically unable to take proper care of herself either during or after her pregnancy. It must not be forgotten that frequently a baby

requires far more physical effort from its mother after it is born than before.

In addition to the physical examination and the patient's history, laboratory studies are a third source of invaluable information. The appropriate extent and character of these examinations will depend largely upon the information elicited by the other two methods of fact finding, although a certain minimal routine is advisable. A serologic test for syphilis, urinalysis and complete cytologic study of the blood constitute the barest minimum. Should the history indicate the probability of previous renal injury, as from scarlet fever or diphtheria in childhood, tests planned to evaluate the kidney functional capacity are indicated.[2] Discovery of anemia, even of low grade, warrants further investigation into its probable cause. These are suggestive illustrations of the comprehensiveness of an adequate health evaluation made prior to pregnancy. The discovery of heart disease likewise makes further study imperative.

The older and traditional pessimistic outlook for all women with heart disease contemplating marriage and motherhood is unwarranted. Yet it is safer to err on the side of conservatism and lay all the facts upon the table; the patient, after all, is the one who must make the final decision. As physicians attempting prophylaxis we can only advise. There are many women who apparently prefer to "diaper their way into heaven" despite emphatic forewarning of the excessive risks of repeated pregnancies. The gift of motherhood must never be denied without good and sufficient reasons. The patient is entitled to know of these reasons so far as her education and intelligence permit her to understand them.

Even more frequent is the problem of deciding the advisability of additional pregnancies in women who have already been pregnant one or more times. If the previous gestations failed in fulfillment because of death of the fetus or the loss of a child, the yearning for motherhood may be greatly intensified. On the other hand, if there are already one or more children at home we must consider these responsibilities in advising concerning the safety of further childbearing. For a childless woman knowingly to "take a chance" involves only her and her husband. For a mother of a family knowingly to subject herself to grave risks (having been conscientiously forewarned) involves far greater responsibility. A great many other factors are also involved, such as the patient's age, the history of difficulties with previous pregnancies and the frequency of her pregnancies. An interval of *at least* two years, and preferably three, should elapse between pregnancies in any woman with previously compensated organic heart disease, no matter how well compensated the heart may be. There is no substitute for time in the processes of readjustment and repair after strain.

When reasons exist to make pregnancy truly hazardous it does not suffice merely to declare: "No (more) babies for you!" The patient is entitled to learn both why and how this is to be accomplished; the physician shirks his responsibilities if he does not give advice regarding contraceptive protection after such a decision.

INCIDENCE AND MORTALITY OF CARDIAC DISEASE IN OBSTETRICS

The incidence of all types of heart disease in obstetric patients is approximately the same as for the same age group in the population as a whole. Statistical reports place this incidence at from 1.5 to 2 per cent. The frequency of rheumatic carditis in young women is definitely greater than among men of similar age. The ratio is about 4:3. Apparently young girls with rheumatic heart disease have a somewhat better chance to reach the age of maturity (and child-bearing) than do boys similarly afflicted.

The great majority of organic lesions of the heart observed in obstetric practice are of rheumatic etiology. Congenital heart lesions, hypertensive disease of the heart, luetic carditis, pericarditis and the rare

instances of coronary arteriosclerosis in the more elderly patients all together represent less than 10 per cent of the total. Functional disorders, including paroxysmal tachycardia, the several arhythmias and thyrotoxic disturbances, are common, but rarely so urgent as organic disease. It is notable that approximately half of the maternity patients with organic heart disease have no knowledge of the cardiac disorder prior to its discovery on prenatal examination. This emphasizes the urgency of popularizing preconceptional examinations.

The direct mortality from heart disease in pregnancy varies greatly in the many reported studies. Among the factors which contribute to the variation in these data are differing diagnostic criteria, incomplete records, and, especially, dissimilar classifications as to the cause of death. One comprehensive statistical survey[4] states that the average immediate death rate among obstetric cardiac patients is 4.3 per cent. Other reports[5] place the mortality between 5 and 10 per cent. These figures are misleadingly low, for the deaths from pneumonia, embolism, sepsis and nephritis in obstetric patients are very greatly increased when pregnancy is complicated by heart disease. Congestive failure accounts for at least 70 per cent of the direct fatalities from cardiac disease in obstetric practice. It is notable that about 75 per cent of the fatal cases survive delivery. In half of these the termination of pregnancy is premature. The greatest number of deaths occur within twenty-four hours after delivery.[4]

The outlook for primiparous and multiparous women with heart disease is not the same. With each successive pregnancy the chronic cardiac patient becomes a poorer and poorer risk. The stress of repeated pregnancies accelerates depreciation of the cardiac reserve. Much of the damage done by pregnancy to a heart previously injured is permanent and irrevocable. This is not revealed at all by the data concerning the immediate mortality. We may conscientiously state, although numerical proof is lacking, that the delayed mortality and morbidity are more significant hazards than the immediate risks. Even with limited follow-up studies, it has been observed[5] that nearly half the patients were definitely worse after pregnancy. It is impossible to estimate accurately just how much the lives of many cardiac patients are shortened by pregnancy and labor, but the total must be considerable. These delayed consequences are rarely seen by the obstetrician; the internist and general practitioner are called upon to attempt the miracle of rehabilitating an irrevocably damaged heart months or a very few years after pregnancy and labor have hastened the onset of failure.

PHYSIOLOGIC CONSIDERATIONS

In normal pregnancy the work of the heart is definitely increased. Under certain abnormal conditions this increment in the cardiac burden is considerably augmented. Undue obesity, arterial hypertension, respiratory disorders, anemia and excessive uterine enlargement (twins or polyhydramnios) are some of the frequent complicating phenomena which add tremendously to the cardiac load. In evaluating the probable increase in work for the heart in pregnancy the likelihood of such complications must not be ignored.

In a perfectly "normal" pregnancy the increment of cardiac labor is considerable, especially during the latter months of gestation, and most particularly during labor. Many factors contribute to this. The minute volume of blood flow from the heart is increased on the average 27 per cent in the last half of pregnancy; in some instances this increase amounts to as much as 50 per cent.[6,7] The blood volume is likewise increased; it becomes from 20 to 25 per cent greater at term than prior to pregnancy.[8] This is due to an increase in both the cell and plasma volumes. There occurs also a very considerable increase in the venous pressure,[7] especially in the pelvic and

femoral veins. The oxygen consumption is increased, both because of the high anabolic activity of the rapidly growing fetal tissue and because the maternal metabolic rate is likewise elevated as pregnancy advances.

The increase in weight which is inevitable in normal pregnancy adds to the cardiac load, particularly upon physical effort. Respiratory exchange is diminished by the handicap of relative diaphragmatic immobility in the later weeks of gestation and by the forced high position of the diaphragm. The vital capacity is diminished, especially just before the relief of the excessive abdominal distention which comes with lightening. Frequently dyspnea on exertion is distressing despite essentially normal cardiac function. Obviously a concomitant anemia, even of slight degree, will greatly augment these additional burdens placed upon the circulatory apparatus.

It is surprising, with the demands placed upon the heart by the purely physiologic changes of pregnancy, that true cardiac hypertrophy does not occur. Repeated clinical and experimental studies indicate that no true hypertrophy does occur. The superficial clinical impression is likely to be that enlargement has taken place in the last trimester of pregnancy, but this is due to the changes in cardiac position engendered by the pressure of the high diaphragm. This displaces the heart to the left; the apex impulse may be as much as an inch beyond the midclavicular line. Although the transverse position of the heart increases the area of cardiac dullness elicited on percussion, there is not a true hypertrophy.

Where pre-existing heart diseases occur, the increased cardiac burdens of pregnancy are prone to induce more serious consequences. Hypertrophy existing before the introduction of these additional loads is accelerated and dilatation and congestive failure are all too frequently induced. Pre-existent heart disease is exacerbated by pregnancy. Intoxication, hypertension, anemia, anoxemia and histanoxia are not infrequent additional insults.

DIAGNOSIS OF CARDIAC DISEASE IN PREGNANCY

Diagnosis consists of far more than merely giving a name to a disorder. This is particularly true of heart disease. A comprehensive diagnosis to be fully useful must include consideration of the *pathology* of the lesion or lesions, the *etiology* and the degree and type of *functional impairment*. Diagnosis therefore has quantitative as well as qualitative attributes. One must also consider whether or not the etiologic factors are inactive or still active, and, if inactive, whether they are likely to be reactivated. Such impression is essential to the proper and intelligent treatment of cardiac problems in obstetric patients.

Examination of the heart may reveal physical findings deviating from the normal without there being any actual disease of the heart. Anemia will cause so-called "hemic murmurs," the raised diaphragm will distort the area of cardiac dullness, and nervous disorders may induce arhythmias in the absence of organic heart disease. It must never be forgotten that the diagnosis of "heart disease" carries with it to the patient a connotation which may cause severe emotional or mental damage. It therefore behooves the physician to be cautious and positive, especially in pregnant patients, who are particularly vulnerable to psychic upsets. The lay public visualizes "heart disease" as a dread malady which strikes its victims down with dramatic and tragic suddenness. The physician more frequently sees in the term the nearly inevitable, though often long delayed, picture of congestive failure with edema and orthopnea.

The criteria necessary for diagnosis of heart disease have been very carefully and extensively reviewed by the Criteria Committee of the New York Heart Association.[9] Extended review of their conclusions is not necessary here, but it should be emphasized that the presence of some one or more of the following pathognomonic evidences is requisite for the diagnosis of organic heart disease:

1. Serious arhythmia, such as auricular fibrillation, flutter, heart block or alternation of the pulse.

2. Diastolic thrills and/or murmurs, together with other evidence of valvular (mitral or aortic) deformity.

3. Increased area of aortic or cardiac dullness with displacement of the apex impulse.

4. Hypertensive disease, thyrotoxicosis, chronic nephritis or signs of arteriosclerosis, with or without hepatic enlargement.

5. The classical syndrome of angina pectoris.

The *anatomic diagnosis* will depend largely upon the physical signs elicited. In pregnant women, especially during the later months of gestation, there are a number of factors which distort the normal physical findings, as already discussed. Special care must be exercised in evaluating the observations. The enlargement of the breasts frequently makes both auscultation and percussion relatively unsatisfactory. Nevertheless, any physician competent to diagnose organic heart lesions in non-pregnant patients is competent to do so in obstetric cases.

Etiologic diagnosis depends largely upon the data derived from the patient's history, although associated physical and laboratory observations are also of great value. Hypertensive heart disease is not observed in the absence of long standing hypertension.[3] Serologic evidence of syphilis is confirmatory when cardiovascular lues is suspected. Determination of the basal metabolic rate may be necessary to determine the etiologic relationship of suspected thyrotoxicosis. But, in obstetric patients, 90 per cent of the cases of heart disease are of rheumatic origin. Careful inquiry is essential to elicit information regarding the frequency, severity, duration and recency of acute rheumatoid manifestations, such as tonsillitis, rheumatic arthritis or chorea. These data indicate the latency or activity of the original infection and thus forewarn as to the likelihood of acute recurrences *during* the pregnancy.

The last part of the diagnosis, the evaluation of the degree of *functional impairment*, is the most important of all. It is upon these conclusions that both prognostic and therapeutic decisions will be based. The recently revised American Heart Association Classification of cardiac functional capacity[9] is indubitably the most useful and pragmatic system of indicating the functional reserve. Patients fall into the following classes of diminishing functional reserve:

Class I. No limitation of physical activity. Ordinary effort induces no distress. Physical findings are the only evidence of heart disease.

Class II (Formerly Class IIa). Cardiac disease patients with slight or moderate limitation of physical activity. Ordinary effort induces discomfort.

Class III (Formerly Class IIb). Patients with cardiac disease with greater limitation of physical activity. Less than ordinary effort induces distress.

Class IV (Formerly III). Patients with heart disease unable to carry on any physical activity without discomfort. Decompensated patients.

Before the World War clinical conclusions about heart disease were derived almost solely from the diagnosis of the anatomic defects. MacKenzie[10] was the first to point out the fallacy of such reasoning and emphasize the importance of the functional capacity of the heart as an index of its ability to carry through pregnancy successfully. The above classification, developed largely through the efforts of Pardee, is a refinement of the original conceptions of MacKenzie.

Cardiac patients falling into Class I are good obstetric risks, barring the coincidental presence of other complications. These patients respond to effort without undue dyspnea or distress. The simplest way of measuring circulatory efficiency and cardiac reserve is to determine the amount of effort necessary to induce dyspnea. It is immaterial just what procedure the physician adopts to determine this,[11] so long as a

routine test is used and he knows the range of response in normal individuals. It is not the severity of the dyspnea which is significant, but the effort required to induce it. This information is frequently most easily and accurately derived from the patient's *history*, for in her daily routine the psychic factors of "a test" are absent and the variations of the reserve from day to day are averaged.

Patients in Class II may go through pregnancy without too grave risks, if they obtain the requisite rest and avoid those exertions which induce distress. They require, however, frequent and conscientious prenatal care. Those women who fall into Class III are poorer risks; frequently they require weeks of continued bed rest in the latter part of pregnancy and must be prepared for the efforts of labor by judicious medical treatment. The maxim "To catch heart failure early, examine patients often" must ever be before one. As the load of pregnancy increases the diminution of avoidable burdens may not suffice to keep the strain within the limits of the cardiac reserve. In such patients cardiac failure may supervene despite constant bed rest.

Decompensated pregnant patients (Class IV) are critically and dangerously ill. Their reserve for exertion is nil. Any additional burden upon the heart, such as surgical interference or labor, may precipitate sudden exitus.

Recalling that as pregnancy advances the labor of the heart increases and that functional reserve is best measured by the response to increased effort, one can readily understand the logic of the clinical rule that *the earlier in pregnancy the signs of circulatory embarrassment arise the smaller is the functional reserve and the more precarious the prognosis.* This axiom is equally valid in considering the margins of safety when preëxisting diseases have reduced the functional reserve of other structures than the heart.[12] Frequent and conscientious prenatal observations are the keystones upon which safety for the pregnant cardiac patient must be maintained.

Certain complications may rapidly and extensively affect the prognosis and require modification of therapy which might be otherwise based on functional impressions alone. Auricular fibrillation, embolic phenomena, activation of infection by bacterial endocarditis,[13] intercurrent systemic infection, the development of arterial hypertension and/or renal disease and the appearance of shock with or without hemorrhage are among the not infrequent complications which may suddenly throw all previous prognostication and therapeutic programs into chaos.

TREATMENT OF CARDIAC DISEASE IN PREGNANCY

All therapy must follow three fundamental principles. These are: (1) therapy directed against the etiologic factors: etiologic therapy; (2) therapy to reduce the physiologic burden of the injured structures to permit of physiologic compensation and repair: rest; and (3) therapy to maintain or improve the tissue nutrition and respiration. In the clinical application of these principles of therapeutics the relative importance and urgency of the three may vary considerably. For example, in thyrotoxic heart disease the etiologic attack through correction of the hyperthyroidism is of the greatest significance. On the other hand, instances of congenital cardiac defects or valvular deformities from long inactive rheumatic endocarditis are not amenable to effective etiologic therapy. Similarly, in congestive heart failure, therapy directed against the remote etiology is of little avail, but rest and the improvement of tissue nutrition and respiration by insuring an adequate glucose[14,15] and oxygen supply are often life saving. For therapy to be fully effective it is essential that none of these three principles be forgotten or ignored. Curative therapeutics depend largely upon correction of etiology. This presupposes accurate etiologic diagnosis. It is illogical to antici-

pate rehabilitation and repair of injured structures unless they are assured of adequate supplies of nutriment and oxygen.

The treatment of Grade I (fully compensated) heart disease in pregnancy is largely prophylactic. The cardiac lesion alone does not justify interference, and natural delivery is the rule. Though these patients may complain of some dyspnea and pedal edema in the last trimester of pregnancy, these phenomena need cause no alarm; they occur in patients with normal hearts. However, even fully compensated cases of valvular disease should be observed carefully and often. Any abrupt acceleration of the basal pulse rate, elevation of the arterial tension, exacerbation of edema or coughing is an indication for immediate restriction of activity.

The opportunity for etiologic therapy is limited. It is important to search for foci of infection, such as alveolar abscesses, which may be adding further insult to the previously damaged myocardium. Dental therapy and extraction during pregnancy are safe. They constitute a lesser evil than the neglect of foci of infection.[1] Though it may not be necessary to curtail the normal activity of these patients, they should be cautioned to avoid unnecessary or violent exertion. The cardiac efficiency certainly is not improved by pregnancy and as the cardiac load increases continuously, the reserve margin is constantly narrowed.

Application of the third principle of therapeutics is often of the greatest prophylactic value. A moderate anemia is a frequent concomitant of pregnancy[16] and any diminution of the hemoglobin content of the blood greatly increases the effects of circulatory handicap. Compensated mitral valvular disease is usually associated with a moderate increase in the hemoglobin over the normal; any fall thereof may be decidedly embarrassing to the heart. Therefore, frequent prenatal check-ups of the hemoglobin and blood counts are highly desirable. Prompt anti-anemia therapy with diet, iron and active liver preparations[17] is indicated whenever depletion begins to appear. It does not pay to wait for severe anemia to add serious complications.

The diet must be adequate, not only as regards protein, carbohydrates, fats and minerals, but also with sufficient vitamin content for both the mother and the rapidly growing fetus. It has been shown[18] that vitamin B_1 deficiency is a causative factor in certain cardiopathies arising in pregnancy and that liberal administration has prophylactic value. Protein restriction is prone to aggravate anemia.

The management of patients with Grade II functional capacity (fairly compensated) involves some new problems. Activity may have to be more restricted to keep the cardiac load at a minimum. More frequent prenatal inventories are desirable. Meticulous attention to secondary potential sources of further cardiac insult is important. Prolonged convalescent bed rest after any mild transient intercurrent infection, such as coryza, grippe and the like, is vitally important if additional damage to the myocardium is to be avoided. The patient must be taught to watch closely for the appearance of warning signals such as undue dyspnea, precordial distress and increasing pedal edema. She *must* stop when these appear. Sometimes periods of complete rest in bed for weeks are necessary to restore circulatory compensation. In Class III (poorly compensated cases with a small margin of safety), hospitalization, absolute rest and nursing care are requisite. Patients in this class must be under constant observation during the postpartum period. All cardiac patients are best kept in bed at least ten (and better more) days before the date of expectancy.

The choice of obstetric procedure in these gravid cardiac cases is often difficult; many factors enter into the decision as to whether pregnancy is best terminated by normal delivery, premature induction of labor, cesarean section or abortion. Of critical importance is the prognostic impression concerning whether the patient is exposed to a greater danger and increased irreparable and irrevocable cardiac damage

if gestation is permitted to continue. Prognostication as to the reserve for the strain of labor is best made at the last possible moment. Labor is often precarious for the cardiac patient; the choice is that of the probable lesser evil. No labor is easy, despite the oft repeated platitude that "cardiac disease patients have easy labors." Labor introduces strains of unpredictable intensity and duration. Of the many factors which must be considered in connection with the choice of method of delivery, the degree of compensation, the arterial tension, the condition of the blood, the pulmonary findings, the obstetric condition of the pelvic passages, the parity of the patient and the skill of the obstetrician are of major importance. Each problem must be considered individually; generalizations and routine management are impossible.

The earlier in pregnancy signs of failing compensation appear, the narrower is the margin of safety. If evidence of failure appears before the sixteenth week, termination of pregnancy by therapeutic abortion is unquestionably the wisest course.[19] The likelihood of survival of either the mother or the fetus in such instances is almost nil; early abortion offers the woman better chance of survival. The borderline cases or patients who refuse such life-protecting measures can occasionally be carried on to the point of fetal viability and delivered well before full term by cesarean section, followed by sterilization. The risks of such a program, however, are very great.[20]

It cannot be overemphasized that *operative procedures should never be undertaken upon decompensated patients (Class IV) without a proper course of medical treatment.* The cardiac condition is more urgent and critical than the obstetric problem. The induction of abortion is never justified during cardiac decompensation.

If labor should begin naturally (either at term or prematurely) in the presence of congestive failure, morphine should be administered in the hope of delaying delivery by the arrest of uterine contractions until the circulatory conditions have been made more favorable by intensive medical therapy.[21] The dread complication of congestive failure arising during labor is often heralded by a sudden fall in the arterial tension and a rise in the pulse and respiratory rates. Such signs are grave indications of impending disaster; the obstetrician must devote his energies to procedures which will ease the strain upon the exhausted heart while the internist combats the circulatory emergency. Pulmonary edema, as evidenced by moist râles in the lung bases, is best attacked by subcutaneous injections of small repeated doses of atropine sulfate (gr. $\frac{1}{150}$ to gr. $\frac{1}{50}$—0.4 mg. to 1.3 mg.). Digitalis should be administered intravenously until full digitalization is attained. Late nausea and vomiting from over-digitalization are better than a fatality due to inadequate dosage.[21] Blood loss should be kept at a minimum. The withdrawal of blood by phlebotomy to relieve congestive failure in an undelivered woman in labor or near term is a practice fraught with danger. The amount of blood which may be lost during labor or immediately thereafter is never predictable. Frequently the edematous uterine tissue of poorly compensated patients bleeds excessively and the risks of exsanguination and shock are superimposed upon those of cardiac exhaustion.

These patients require *constant* attendance, not only during labor, but for many hours thereafter. As has been mentioned previously, the majority of cardiac deaths in obstetric practice occur in the puerperium. For those patients with lowered cardiac reserve delivery should be by the method involving the least effort on the part of the patient. In competent hands cesarean section under local anesthesia is often the safest course. The patient should be propped up, no matter what the method of delivery, and delivered in a semi-recumbent position. This is especially important when mitral disease makes pulmonary edema a serious hazard. If delivery is by cesarean section, the patient should be sterilized at the same time; the

brief prolongation of operative manipulation adds little to the already grave risks. Further pregnancies must be avoided by some means. If sterilization of the woman or her husband is impossible or unwise, adequate contraceptive advice is urgently needed before these patients are discharged.

One aspect of medical therapy deserves special attention: the administration of oxygen. Oxygen is invaluable as a means of enhancing tissue respiration and improving the nutrition and strength of the myocardium. It has often been stated that "when cyanosis appears, oxygen therapy is indicated," but such advice is far too conservative. Early and prolonged inhalation of oxygen does no harm and may do immeasurable good in preventing cardiac default. It is hardly logical to expect efficient work from muscular tissue (both myocardial and myometrial) which must labor under conditions of inadequate oxygen tension. It must be recalled that even though there may be little gross anoxemia, nevertheless histanoxia (cellular tissue ischemia) is inevitable in circulatory failure. An elevated oxygen tension of the arterial blood is thus desirable.

The second stage of labor is the most exhausting. The physical effort is great and often protracted. Forceps delivery and/or episiotomy may reduce this burden. Ethylene is the anesthetic of choice from the internist's viewpoint. Ether may readily cause aggravation of the pulmonary edema associated with passive congestion.

Puerperal care is of the greatest moment in reducing the mortality and morbidity of cardiac damage. There need be no haste in removing the postpartum patient from the delivery room. She should be kept under close scrutiny for hours. Warmth, rest, oxygen and fluids are antidotal to postpartum shock. Hypodermoclysis of physiologic saline solution is somewhat safer than intravenous injection of fluids, unless the latter are administered very slowly. Where extensive blood loss has occurred several small (250 c.c.) transfusions of whole blood are desirable; not only do these replace the loss in volume, but they offer replenishment of the reduced hemoglobin content of the blood. Oxygen does little good unless there is hemoglobin to carry it to the vital tissues. Oral ingestion of fluids, like parenteral administration, should be limited to small quantities taken frequently. These patients should never be dehydrated by restricting fluid. Such advice for the control of edema is mentioned only to be condemned. This applies to all edematous states, whether of circulatory[15] or renal origin.[3] But fluids must be given cautiously, a little at a time. Too rapid absorption of fluids may precipitate a rapidly fatal pulmonary edema.

SUMMARY

In such a brief résumé of the problems of heart disease in pregnancy it is possible to touch only briefly upon the more urgent aspects and to attempt to provoke an active curiosity about these questions. Generalizations are dangerous. There are very many variables which make each case a wholly individual problem in diagnosis, prognosis and management. The urgency of the clinical picture is frequently obscured by economic, emotional and sociologic factors. The functional capacity of the heart, as indicated by the response to stress on increased effort, remains the most reliable single criterion of prognostic import. The therapeutic management depends largely upon the prognosis, for the keystone of the whole structure of treatment of these patients is prophylaxis. To avoid cardiac failure, or postpone it as long as possible, is the objective in treatment of organic heart disease, irrespective of the anatomic lesion and regardless of pregnancy. Therefore the question of future pregnancies in either nulliparous, primiparous or multiparous women is an integral part of the problem. Preconceptional health evaluation and determination of functional reserves is the prime prophylactic measure. The right to bear children should never be denied without sufficient cause. The outlook may be greatly improved by intelligent

and whole-hearted coöperation between patient and physician during the prenatal period. Neglect and the assumption that the appearance of symptoms of failure will give sufficient warning for the institution of active therapy are dreadfully dangerous. The price of security is constant watchfulness.

Therapy to control the cardiac disorder must include application of all three of the cardinal principles of therapeutics: (1) etiologic therapy; (2) reduction of the physiologic burden of the injured structures; and (3) assistance to tissue nutrition and respiration. Of these three, the last is the most frequently neglected. It is the patient, not the disease, that is the physician's concern. Before giving any advice or making any decision, no matter how trivial or how serious, one must weigh the probable benefits against the probable detriments. If they are about equal, have the courage not to interfere.

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ECTOPIC PREGNANCY*

A REVIEW OF 137 CASES

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NEW ORLEANS, LOUISIANA

NO chapter in gynecology is fraught with more interest and historical romance than that of ectopic, or extra-uterine, pregnancy. Woman, from the very beginning, was undoubtedly subject to the wayward migration and the aberrant implantation of a fertilized ovum with the consequent tragic sequelae; however, the writings of the ancients do not mention the condition. Sixteenth century investigators gathered reports of the occurrence of lithopedions, as well as of instances in which ulcers formed at or near the umbilicus or in the cul-de-sac, which upon dilatation permitted the escape of skeletal remains of a fetus along with putrid material. These cases comprised only that small group which we know today as primary ovarian or abdominal pregnancies, or those in which a tubal abortion has occurred and the fetus has been able to find a partially suitable site of nidation on the abdominal viscera with survival for varying periods of time. These early accounts do not take into consideration that large and important class of cases which we recognize today as early unruptured or ruptured tubal pregnancy. Diagnostic acumen and surgical skill had not yet developed to that point where the true pathology could be interpreted or proper treatment could be formulated.

Recognition that extra-uterine pregnancy is not a rare and bizarre condition paralleled the growth of abdominal surgery. Even in 1876, Parry warned the profession that, "Operative interference is condemned by the highest authorities upon the subject, and he who would subject a woman under these circumstances to the dangers of gastrotomy would have to possess the courage of McDowell and his immediate followers." Parry collected 500 cases of ectopic pregnancy, the total number which had appeared in the literature up to 1876; of these 366 patients died and 163 recovered, a mortality of 67.2 per cent. It was not until almost the dawn of the twentieth century that operative interference was acknowledged as the treatment of ectopic pregnancy, for Lawson Tait, in 1883, was the first to perform the operation for ruptured tubal pregnancy, and although the first patient died, he correctly attributed his failure to faulty technique. Of the next forty patients only one died.

This present study comprises a review of all the cases of ectopic pregnancy which occurred at Touro Infirmary, New Orleans, during the years 1924–1936, inclusive. One hundred and forty-six histories were obtained, but nine of these were discarded because in five instances the patients were discharged without operation, and consequently, the diagnosis was not proved; and in four instances the operative notes and the absence of confirmation by the pathologist did not seem to justify the diagnosis of ectopic pregnancy. Three of these cases had been erroneously recorded as ovarian pregnancies, and the fourth was discarded because it did not seem to be a true interstitial pregnancy, for the pathologist reported a normally pregnant uterus.

A study of the statistics of ectopic pregnancy reveals an apparent increasing frequency of this condition. Older textbooks, written before 1900, give the proportion of extra-uterine to intra-uterine pregnancies in figures which vary from 1 in

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500 to 1 in 1200, whereas Wynne in 1919 reported 306 cases of ectopic pregnancy among 22,688 patients in the gynecologic clinic of Johns Hopkins Hospital, an incidence of 1.3 per cent of all gynecologic patients seen (Schumann).

Schumann found a ratio of one ectopic pregnancy to every 267 normal and stillborn deliveries in the city of Philadelphia during the year 1918 (.38 per cent). To make allowance for those patients with ectopic pregnancy who are not admitted to hospitals, some of whom die at home under a mistaken diagnosis, and a few of whom recover without the aid of treatment, 10 per cent was added to the total reported cases, and, in consideration of the fact that all intra-uterine pregnancies do not go to term, and that approximately one abortion occurs for every four full term pregnancies, 25 per cent was added to the total number of births. The above figures, corrected in this manner, give a ratio of one ectopic pregnancy to every 303 normal pregnancies (0.33 per cent).

To obtain the relationship of extra-uterine to uterine pregnancy in New Orleans, 865 cases of ectopic pregnancy were collected, which had occurred in the seven hospitals located in the city during the years 1924–1936, inclusive. During these same years, 124,498 live births and 5,793 stillbirths, a total of 130,291 births, was reported. This reveals an uncorrected incidence of one extra-uterine to every 151 intra-uterine pregnancies (0.66 per cent). If these figures are corrected, according to the method used by Schumann, the incidence becomes one ectopic in every 171 pregnancies (0.59 per cent). This is the highest incidence of ectopic pregnancy which has ever been recorded in any locality.

It is extremely doubtful if the high incidence revealed by these figures represents an actual increase in the frequency of this condition. There are two facts to be noted in this connection: (1) the colored population of New Orleans is large and it is well known that the pelvis of the colored woman is more subject to specific infection with its attendant damage to the adnexae than is that of the white woman; and (2) a large proportion of the work done in New Orleans' hospitals comes from outlying sections where no hospitals exist, emergency cases being rushed to Charity Hospital and other institutions in New Orleans. It is very likely, moreover, that the apparent increase in incidence simply represents the increasing frequency with which the condition is diagnosed, and demonstrates a marked improvement in medical skill and education of the physician.

TABLE 1

ECTOPIC PREGNANCIES IN THE HOSPITALS OF NEW ORLEANS

(1924–1936 inclusive)

Charity Hospital	486
Baptist Hospital	83
Touro Infirmary	146
Hotel Dieu	52
Mercy Hospital	38
French Hospital	23
N.O. Dispensary	36
Flint-Goodridge	1
	865 cases

BIRTHS IN THE CITY OF NEW ORLEANS

(1924–1936, inclusive)

	Live Births	Stillbirths
1924	10,870	555
1925	10,239	526
1926	10,441	504
1927	10,463	542
1928	10,123	553
1929	9,383	401
1930	9,339	396
1931	9,207	321
1932	9,154	429
1933	8,532	407
1934	8,825	338
1935	8,959	403
1936	8,963	418
	124,498	5,793
Total	130,291	

The youngest patient in this study was 17 years of age and the oldest was 43 years. The largest number of cases, 65.2 per cent of the total, occurred in the decade 24 to 33.

Since implantation, conceivably, may occur at any point along the path followed

by the ovum in its migration to the tube, it follows that ectopic pregnancy may vary greatly in location. Such variations are common and are responsible for the classification of this abnormality according to the original site of implantation into three primary groups:

1. Ovarian
2. Tubal
   (*a*) Ampullary
   (*b*) Isthmial
   (*c*) Tubo-ovarian
3. Interstitial

Table II
AGE INCIDENCE

	No. of Cases	Per Cent
Not given	6	
17 years	1	
18 years	2	
19 years	3	
20–24 years	21	15.3
25–29 years	57	41.6
30–34 years	33	23.6
35–39 years	13	9.48
40–43 years	1	
	137	

Two other types of primary ectopic pregnancy, namely, cervical and abdominal, have been mentioned in the literature, and for the sake of completeness should be considered. Primary abdominal pregnancy would result if the ovum was fertilized while free in the abdominal cavity and was implanted upon any abdominal viscus. While this is theoretically possible, and while some few cases have been reported as such, the existence of abdominal pregnancy as a primary occurrence has never been proved and is extremely doubtful. Secondary abdominal pregnancies, although relatively infrequent, do occur and were the first cases of extra-uterine gestation to be recognized. Cervical pregnancy is occasioned by the implantation of the fertilized ovum in the cervix uteri, and although a few cases have been reported in which the cervix was undoubtedly the site of original implantation, the condition probably arises most frequently from detachment of a normally imbedded ovum with subsequent reimplantation in the cervix. It seems more logical to consider it as a variety of uterine, rather than as on extra-uterine gestation.

The comparative frequency with which these primary forms occur cannot be accurately determined because, too often, the surgeon's notes make no reference to the location of the pregnancy and, as a rule, no attempt is made to trace a secondary ectopic pregnancy, when encountered, back to the primary form from which it originated. The published statistics of this condition, for these reasons, do not often mention the anatomic location. In analyzing the groups of cases reported in the literature, it can be seen that tubal pregnancy constitutes the large majority of cases, and that ovarian and interstitial pregnancy are both uncommon and occur with approximately equal frequency. In analyzing the 137 cases which form the basis of this study, very similar proportions are revealed.

Type	No. of Cases	Percentage
Tubal	134	97.9
Interstitial	2	1.4
Ovarian	1	0.7

It is commonly believed by a large number of the medical profession that the right tube is more often affected than the left, and many reasons have been advanced to explain such an inequality. The most frequently advocated explanation is that the right tube is commonly damaged by acute appendicitis, and hence becomes a suitable site of ectopic gestation. The lateral dextrotorsion of the uterus is also claimed to explain the more common occurrence on the right side, but it is doubtful if any such relationship can be proved. Some authors have stated that the right tube is usually longer than the left, and that this increased distance, traversed by the

ovum on its way to the uterus, favored the development of pregnancy in the tube. This statement cannot be substantiated. Schumann is one of the few who expresses doubt concerning the greater frequency with which the right tube is involved and believes, from a review of his own statistics that but little variation occurs. Table III, from Schumann, supplemented by the present study and representing a total of 876 cases, reveals that a small series of cases may show a greater preponderance in either the right or left tube, but that a large group, as represented by the total, shows practically an equal distribution.

TABLE III

Author	Right Tube	Left Tube	Both Tubes
Oastler	54	46	2
Farrar	148	140	1
Bovee	28	31	0
Frank	23	29	0
Foskett	43	74	0
Williams	69	53	1
Present study	77	56	1
	442	429	5

Many factors of a varied nature can be held responsible for the production of ectopic pregnancy, but the difficulty lies in fitting any one of a number of theoretical or actual possibilities to the given case. In discussing this matter, it is best to consider separately the etiologic factors for the different forms.

Primary abdominal pregnancy has never been proved, and, since it exists chiefly as a theoretical possibility, it is not surprising that any explanation offered for its occurrence is purely hypothetical. It is thought that the presence of endometrial transplants, or of aberrant decidua, such as is quite commonly found in normal pregnancy, upon the peritoneal surfaces of many organs, might favor such an eventuality. It is a doubtful possibility and it is certainly best to consider both the occurrence and the explanation of primary abdominal pregnancy as outside the realms of practical thought.

Ovarian pregnancy is a proved possibility, and since Schumann, in 1921, reported a total of forty-three cases, the number is being added to with increasing frequency. For gestation to occur in this location, it is absolutely necessary for the ovum to be fertilized while it is still in the graafian follicle. It has been suggested by Leopold that a centrally located follicle may rupture into a superficial follicle, which has just extruded an ovum. This communication between the two must, perforce, be large enough to admit spermatozoa from the superficial follicle, and yet small enough to prevent the expulsion of the ovum from the deeper follicle. The existence of a perioöphoritis, with a resulting thickened tunica albuginea, could account for the stigma in normal ovulation meeting these requirements in size. Suffice it to say that the existence of ovarian pregnancy is definitely known, but its production is questionably explained.

Tubal pregnancy, by far the most common form, possesses a proportionately greater number of explanations and, from a mass of theory and clinocopathologic facts, the causative agents as listed by Schumann are generally accepted:

1. Obstruction of the tubal lumen from without.
2. Obstruction of the tubal lumen from within.
3. Anomalies of the tube, such as accessory ostia and congenital diverticula.
4. External migration of the ovum.
5. Decidual reaction in the tube.

Peritubal adhesions are the most common cause of obstructions located outside the tubal lumen. They frequently follow a perisalpingitis of extra- or intratubal origin, or an inflammation secondary to appendicitis, diverticulitis, or a general peritonitis following rupture of some abdominal viscus. Conservative operations for the relief of these very lesions may leave the tube more, rather than less, susceptible to

ectopic gestation. Giles, from a group of 125 cases, reported that 24 per cent of women who became pregnant after conservative surgery of this type had extrauterine gestations. Even the correction, by suspension, of retrodisplaced uteri may, in the absence of tubal pathology, predispose to this development, as was revealed by P. W. Siegel, who found that 15 per cent of his seventy-three patients ectopically pregnant became so after suspension of the uterus. Other gynecologic operations apparently have little influence in this direction. The presence of a tumor in some neighboring tissue may also obstruct the tubal lumen from pressure and favor implantation of the ovum. Plastic operations upon the tube, performed either to produce sterility or to relieve it, frequently are followed by ectopic gestation. Spontaneous torsion of the tube, though a rare occurrence, can obstruct the lumen of the tube and represents a factor which should be included in this group. Numerous cases proving the occurrence of all these factors have been reported.

Salpingitis, particularly of gonorrheal origin, is the morbid process usually responsible for obstruction of the tubal lumen from within. Williams found evidence that an inflammatory reaction had preceded ectopic pregnancy in all his specimens. When both tubes were removed, these changes were proved microscopically to be bilateral, and diverticula were found not only in the pregnant tube but in the opposite one also. Other factors, not inflammatory in origin, which can obstruct the lumen from within, can be mentioned. Katz believes that the cyclical changes demonstrated in the tubal mucosa during menstruation and pregnancy can result in a heaping up of the epithelial cells on each other to such an extent that mechanical obstruction may result. Rubin has also shown the existence of spasm in the tubal musculature, and has revealed that pressure, much greater than normal, is necessary to overcome such resistance. Such a spasm, with an absence of normal peristalsis, could readily interfere with the progression of the ovum.

Diverticula, similar in all respects save in inflammatory reaction to those produced by salpingitis, have been commonly found in the Fallopian tubes. Their existence is predicated upon an abnormality in the embryologic canalization of the lumen. Accessory ostia and accessory tubes likewise represent pockets in which the ovum may be trapped. A persistence of fetal characteristics, i.e., excessive length and more numerous convolutions, increases the distance to be traversed by the ovum and may also interfere with tubal peristalsis. Both of these factors predispose to ectopic pregnancy.

Increase in the size of the ovum, rather than narrowing of the tubal lumen, could prevent the ovum from reaching the uterine cavity. Such an occurrence can be explained by external migration of the ovum. This term is used to describe the wandering of a fertilized ovum from one ovary across the pelvic cavity to enter the tube of the opposite side. The increase in size of the ovum results from growth during the greater length of time required for such a journey. Cases have been described in which no other mechanism, aside from external migration, could explain their occurrence. It is not, however, believed to be a frequent factor.

The occurrence of a decidual reaction in the tube is believed by many to be the most important contributory factor, for it would invite attachment and implantation by any ovum with which it came into contact. Such a decidual reaction can result from the presence of endometrial transplants in the tube or from an actual decidual response in the tubal mucosa. Döderlein and Herzog have reported a case of ectopic pregnancy located in an adenomyoma of the uterine wall, proving beyond all doubt the existence of this factor. Actual decidual response in the tubal mucosa has been demonstrated to occur in normal pregnancy by many investigators. It is regarded by some as an evidence of functional degener-

acy with reversion to a lower type. Frankel and Schenck have found decidual tissue to be present in the tube of 87.5 per cent of specimens of ectopic pregnancy which they have examined, and Kermauner has demonstrated decidua in the tubes of 15 per cent of a series of normal pregnancies. These findings suggest that some other factor other than tubal obstruction may play the essential rôle. It is probable that tubal obstruction must occur in association with a complementary influence, which would create a favorable soil for implantation, in order for ectopic pregnancy to result. A decidual response in the tubal mucosa can well answer this purpose.

An attempt to determine the etiology of the 137 cases collected for study was hindered by the scarcity of information recorded in the hospital histories. Only those factors mentioned in the pathologic report were found useful. The microscopic study of those cases reaching the laboratory revealed the presence of salpingitis, a definite etiologic factor, in twenty cases (14.6 per cent). A review of the operators' notes located three cases which may possibly have resulted from external migration of the ovum. A decidual response in the tubal mucosa was rarely noted.

In considering the eventual termination of any extra-uterine pregnancy, it should be remembered that three essential possibilities can occur: (1) early death of the fertilized ovum with complete resorption; (2) development of the fetus to term, or else to an advanced state, in its site of original occurrence, with the possibility of delivery by laparotomy, or if retained, death followed by such terminal changes as suppuration, skeletonization, lithopedion formation, or saponification; (3) rupture. If rupture results, three developments may take place: (1) the embryo may die; (2) the embryo may become reimplanted and continue to grow; (3) the placental attachments may survive at the primary site, and the fetus, its position changed, continues to develop.

Regardless of the manner in which rupture occurs, and regardless of the variety of ectopic pregnancy involved, hemorrhage into the peritoneal cavity of the mother is almost universal and is frequently copious. If this hemorrhage is very profuse and rapid, exsanguination of the patient prevents the occurrence of further changes. However, if the bleeding occurs slowly and in smaller amounts, especially if the lesion is a tubal abortion, the blood may gravitate into the cul-de-sac and become partly organized. The presence of blood in the peritoneal cavity incites an irritative, plastic, aseptic peritonitis, and the collected blood becomes walled off by adhesions, forming a hematocele. Hematocele represents a favorable termination of ectopic pregnancy, for it predicates the passage of sufficient time for hemorrhage to have ceased and the chances of exsanguination to have passed. It is not without its dangers, however, for the collected clot and free blood may become infected and form a pelvic abscess.

	No. of Cases	Ruptured	Unruptured	Not Stated
Right tube	77	56	20	1
Left tube	56	36	15	5
Bilateral	2	2	0	0
Ovarian	1	1	0	0
Cornual	1	0	1	0
	137	95 69.4 per cent	36 26.2 per cent	6 4.4 per cent

The scarcity of information in the hospital records, particularly in the surgeons' notes, is again revealed when an attempt is made to analyze the present study as to termination. Frequently, the condition of the tube at operation was not described, and hence, it was impossible to determine whether tubal abortion or tubal rupture had taken place. One abdominal pregnancy, secondary to tubal rupture, occurred in which the embryo had become reimplanted upon the anterior wall of the

rectum. For the whole series, it was possible to divide the cases into ruptured and unruptured groups only. Those cases classed as unruptured were, in all probability, tubal abortions, although the information furnished was not sufficient to justify calling them so.

Before rupture occurs, no symptoms exist aside from those common to early uterine pregnancy, such as amenorrhea, nausea, vomiting, soreness of the breasts, and frequency of urination. Occasionally, a vague sensation of discomfort or soreness may be noted upon the affected side. Amenorrhea is not always constant, but when present, usually leads the woman into a false belief that she is normally pregnant. Vaginal examination before rupture may reveal a slight softening of the cervix and perhaps a slight enlargement of the uterus. However, changes in the size and consistency of the affected tube are indefinite and of little specific diagnostic significance.

The absence of unusual symptoms is responsible for the fact that extremely few women consult a physician during this period, and the lack of any characteristic physical signs results in a failure correctly to diagnose those cases which do present themselves. No clinical alterations occur in the blood or urine, and, although the Friedman test is positive, an early normal pregnancy is suspected. The diagnosis of an unruptured ectopic pregnancy during early development is attended with the same luck which blesses the golfer who scores a hole-in-one.

When rupture does occur, the history is extremely important if a correct diagnosis is to be made. Usually, there will have occurred a period of amenorrhea of one month's duration or longer, followed by "spotting," or even by vaginal bleeding of a more frank nature. There are two important characteristics of this bleeding which should be noted: it occurs at a period which is not in rhythm with the regular menstrual cycle, and it is most often of a dark brownish black color.

A period of amenorrhea does not always preëxist before rupture. No period may have been missed, but it may have been delayed a few days, or careful questioning will reveal that the last menses were very scanty and not entirely normal. This "irregularity" of menstruation, whether associated with amenorrhea or not, is one of the most important and frequent symptoms. Rarely, ectopic pregnancy may proceed to rupture without any noticeable menstrual disturbance, but in such a case there is always a question of the care with which the history was taken.

A history of amenorrhea preceding the onset of symptoms is recorded in seventy-two of the present series of 137 cases (52.8 per cent). The information is vague on this point in many of the histories. Where a provisional diagnosis of some other condition than ectopic pregnancy was given, there is very seldom mention of a period of amenorrhea. A history of abnormal vaginal bleeding was recorded in 111 cases (81 per cent). This bleeding continued until the operative day in some cases and was intermittent in others. Five patients expressed a belief that they had passed the products of pregnancy. In ten cases, a dilatation and curettage had been performed previous to admission; in twenty-two, curettage was performed at the time of operation. Throughout the series, abnormal bleeding is often reported as a normal menstrual period. The information on these two symptoms, amenorrhea and bleeding, is more confusing and less accurate than on any other phases of the syndrome. There were twenty-six patients in whom no history of bleeding was recorded. Fifteen of these were in shock at the time of admission. Careful inquiry, after operation, might have altered this finding.

Pain in the pelvis, usually recurring in a fairly definite cycle, is the next most important point in the history. It may be sudden, severe, and lancinating in type, or may, in its incipiency, resemble menstrual cramps. An analysis of the frequency of the various

symptoms in the series revealed that only six patients suffered no pain. The absence of pain was definitely stated in the history of five of these, and, in one, pain was not mentioned as a symptom. In the majority of cases where rupture occurred, pain was sudden and severe, but in some instances was preceded by cramps in the lower abdomen. Occasionally, pain was the initial symptom and occurred without relationship to an irregularity in menstruation. Radiation of pain to the thighs, back, and chest was noted. Shoulder pain occurred in thirteen cases. The frequency with which rupture occurs in the bathroom is a finding that impresses the investigator of a series of cases. Intraabdominal pressure is increased by straining during urination or defecation, and this force applied to a tube distended to its fullest extent results in immediate rupture.

The onset of sudden pain was accompanied by fainting or by several fainting spells in nineteen cases, and thirty-one complained of a feeling of faintness or weakness, which made a total of fifty cases with symptoms of syncope (36.4 per cent). Forty-one patients (29.9 per cent) were in a state of shock at the time of operation, and in most instances this meant at the time of admission. There were a few patients upon whom operation was delayed, in the absence of the correct diagnosis, who went into shock during their hospital stay.

Nausea, or both nausea and vomiting, were present in fifty-five cases (40 per cent). As a rule, it began with the onset of pain and was not noted as an accompaniment of the pregnancy until the acute symptoms manifested themselves.

Cullen's sign was recorded in only one case, although it was looked for as a diagnostic sign in many instances.

Upon physical examination, the most universal finding was tenderness in the lower abdomen, which was present in 111 cases (81 per cent). Both quadrants of the lower abdomen were equally painful in forty-four cases (32 per cent). Tenderness was more marked on the right in forty-eight cases (35 per cent), and on the left in nineteen cases (14 per cent), although in some it was present in a lesser degree on the opposite side also. In twenty-six cases (19 per cent), there was no tenderness in the lower abdomen. Eight of these were in shock at the time of examination, and in eleven the tube was unruptured. There were several patients who complained of tenderness in the gall-bladder region as well as in the lower abdomen. Tenderness was present very often in the absence both of rigidity of the abdomen and of a palpable mass.

Rigidity was found in only fifty-seven cases (41.6 per cent). In some, the rigidity was slight, and in many was evident only upon deep palpation. In others, the whole abdominal wall was tense and "rigid as a board." The tube was ruptured in all but six of the fifty-seven cases with rigidity; in three of the six, there was only slight rigidity; in five of the six, a mass was also palpable.

In fifty-four of the 137 cases, a mass was palpable. It was located in the right lower quadrant in twenty-eight cases (20 per cent; in the left lower quadrant in fourteen (11 per cent); in the posterior cul-de-sac in six (4.5 per cent); in the midline in five (4 per cent); and occupying the whole pelvis in one case (0.7 per cent).

Examination of the blood, after rupture, reveals changes which are dependent upon the amount of intraperitoneal hemorrhage. Recent profuse hemorrhage was shown by Farrar to cause a marked leucocytosis, whereas, in milder types, the leucocyte count may show no change. The red cell count and hemoglobin are directly related to hemorrhage and fluctuate accordingly. The urine, scanty in amount because of the loss of body fluids, shows no changes unless hemoglobinuria, resulting from intraperitoneal hemorrhage, is demonstrated. The Friedman test may be positive or negative according to the viability of the trophoblast.

The statement is often found in the literature that a relative sterility of long duration usually precedes the development of ectopic pregnancy. This is not borne out in the present study, for sixty-two of the 137 women were found to have been previously pregnant. (Table IV.) Of these sixty-two women, twenty-three had had three or more children; no statement was made in forty-four histories.

Table IV
Previous pregnancies in 62 cases

No. of Cases	No. of Pregnancies
23	1
16	2
7	3
4	4
4	5
5	6
1	8
2	9
62	38

In sixty-five of the 137 cases (47.2 per cent), the diagnosis of ectopic pregnancy was correctly made. In thirty-two cases (23.5 per cent), the diagnosis was thought to be ectopic pregnancy or some other condition. In forty cases (29.3 per cent) the diagnosis was entirely erroneous. If these cases, in which the possibility of ectopic pregnancy was weighed against some other condition, are added to those in which the diagnosis was unequivocally correct, the resulting percentage, 70.7 per cent, of accurate diagnoses parallels closely that found by other investigators.

The dictum that all cases of ectopic pregnancy should be subjected to operation as soon as possible, regardless of the patient's condition, should be the unvarying rule for every physician who makes such a diagnosis. The inability to foretell the result of an internal hemorrhage, and the suddenness with which rupture can occur, are factors which make this rule just as applicable to the woman who with an early unruptured tubal pregnancy has no symptoms as it is for the patient in grave shock from excessive bleeding. There is no such thing as expectant treatment for extra-uterine gestation because the prognosis becomes more serious the longer operation is delayed. Hunter Robb's statement, based upon experimental surgery in dogs, that intra-abdominal hemorrhage is seldom, if ever, the cause of death, cannot hold water when contrasted with the statistics collected by Parry. Parry collected the records of 500 cases of ectopic pregnancy with 386 deaths. Of the total number of deaths, 174 (52.8 per cent) resulted from hemorrhage following rupture. Of these 174, the duration of life after rupture is mentioned in 113. Of these 113, 71.7 per cent were dead within twenty-four hours, and only 13 per cent were alive after forty-eight hours. These figures alone should impress everyone with the necessity for haste in the treatment of this condition.

No time should be wasted before surgery by transfusion or infusion in an attempt to rally these patients. Such procedures can be accomplished during the progress of an operation, and the patient will benefit greatly from the time saved. Cases can always be recalled in which death occurred, without operation, while valuable time was lost in a search for blood donors, or in a period of "watchful waiting" for the general condition of the patient to improve. On the other hand, it is customary to note a marked improvement in the pulse of a gravely shocked patient as soon as the bleeding vessels have been ligated at operation, despite the fact that no fluids or stimulants were administered. It is well to repeat that the time for the administration of fluids is during, or after, the control of the hemorrhage by ligature.

The extent of the operative procedure is limited by the judgment of the surgeon and by the patient's condition. If hemorrhage has been severe, its control by removal of the affected tube is all that can be asked. If the blood loss has been slight, and the patient's condition warrants it, the remaining tube should be carefully inspected and, if evidently diseased, removed. The extravasated blood is best left in the patient's

abdomen for eventually it is absorbed and attempts to remove it increase the length of the operation. No more surgery should be practiced upon the victim of a ruptured ectopic pregnancy than is absolutely necessary to insure a primary postoperative recovery. He who under such circumstances, incidentally removes the "chronic appendix," or suspends the uterus, or explores the abdomen after removing the affected tube will increase his operative mortality by a great percentage.

In a certain number of cases, ectopic pregnancy recurs in the remaining tube. Smith studied 1,608 cases operated upon by members of the American Gynecological Society and found fifty-eight repetitions (3.6 per cent). In five of the 137 cases (3.6 per cent) from Touro Infirmary, a previous ectopic pregnancy had occurred. The percentage incidence in these two series is the same.

Three deaths occurred in the series of 137 cases. This represents a mortality of 2.18 per cent, which compares most favorably with that of 7.7 per cent reported by Schumann. Mortality, in any condition, is dependent upon the skill of the physician, but it is estimated that the average mortality in the better hospitals will be 4 per cent, or under. The operations in the present study were performed by forty-three different surgeons and this fact precluded the possibility of follow-up by this investigator.

In 1937 . . . fetal and neonatal deaths aggregated 142,500. This is more than the number of deaths occurring among individuals in the age group of five to twenty-nine years (132,000) and is approximately 10 per cent of the total deaths for all ages and all causes (1,450,000).
From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

THE TREATMENT OF ABORTION*

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THE etiology of abortion is very important in the prevention and treatment of this condition. Improved social and economic conditions and education in contraception will reduce the number of self-induced and criminal abortions, with the associated high rate of invalidism and mortality. In a review of 1,000 abortions, 65 per cent of induced abortions were in single women and 35 per cent in married ones. The intelligent woman will have pelvic pathology corrected before conception and even before marriage. Pregnancy is not likely to continue in a uterus that bleeds profusely or irregularly, in one that contains a submucous or intramural fibroid to interfere with development of the placenta or the nourishment of the fetus, or where there is a hyperplasia of the endometrium preventing proper nidation of the ovum and suggesting ovarian hormone disturbance.

At the first prenatal visit, the patient should be asked to coöperate in the prophylaxis of abortion. She should be impressed with the necessity of avoiding violent exercise, excessive fatigue, highly emotional states, long automobile rides over rough roads and sexual intercourse during the first trimester. Previous history of abortion, in the absence of well defined cause, suggests the following treatment: bed rest, sedatives, particularly barbiturates, at the time of an expected period, and again at six, eight and twelve weeks' gestation.

Spotting with a dark brown, odorous irritating discharge, without cramps is common in early pregnancy, before the womb is entirely filled and the space between the reflexa and vera is closed. At this time the endometrium that is not covered completely is very vulnerable and is apt to bleed from any condition that causes excessive pelvic congestion such as constipation, fatigue, sexual intercourse, and emotionalism. The same type of bleeding, with the addition of vague cramps or more active bleeding with or without contractions indicates that *abortion is threatened.* Cramps in the lower abdomen without blood are difficult to differentiate from colic, but the absence of diarrhea, constipation or meteorism and urine tests negative for pus or blood indicate the necessity of strict treatment. One must consider, in the absence of cramps, the possibility of the origin of bleeding from an erosion or polypus of the cervix.

Essential treatment for threatened abortion consists of (1) absolute bed rest; (2) ice-bag to lower abdomen; (3) raising the foot of the bed 8 to 12 inches; (4) no cathartics or enemas for three days, then oil retention enema; (5) pelvic examination, through rectum only, if absolutely indicated. (6) sedatives: phenobarbital 1½ gr. b.i.d., codeine ½ gr. with aspirin gr. 10 if pain is present, however mild; morphine, except in large doses, may stimulate contractions; (7) thyroid, if there is evidence of hypothyroidism; (8) wheat germ oil, 2 to 6 c.c. daily in capsules of 1 c.c. each; (9) progesterone 5 to 15 mg. daily. This treatment should be continued until the cramps and bloody discharge disappear. Determine the latter, if not visible, by inserting a cotton probe into the vagina.

Bed rest should continue for at least five days after bleeding has ceased. The treatment of threatened abortion is deterrent while that of inevitable and complete abortion is provocative. About one-third of threatened abortions will recur after all symptoms have subsided. Unfortunately

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there are no definite clinical signs to show that a recurrent threatened abortion will go to term. There is evidence that vitamin E is concerned with thyroid activity and has a relationship to normal pituitary and ovarian function. Doses of wheat germ oil containing vitamin E are given in amounts as high as 15 c.c. daily. This dosage does not seem advisable since the ill effects of hypervitaminosis have been proved for some other vitamins, particularly vitamin D.

Progesterone prevents uterine contractions by opposing the estrin effect of sensitizing the uterine muscle.

Completed abortion is indicated by a closed cervix, more or less complete reduction of the bloody discharge, decreased size and greater firmness of the uterus and absence of pain in the lower abdomen. It is definitely established if the complete ovum is observed. If bleeding recurs after the use of ergot or if bright red blood reappears, the abortion is probably not complete. The treatment is bed rest of four to ten days, depending upon the duration of the pregnancy.

Inevitable and incomplete abortion is termed febrile or afebrile if the highest daily temperature is above or below 100.4°F., respectively. Each requires different treatment, expectant in febrile cases and active in afebrile, allowing an interval of five days of normal temperature to elapse before evacuation of the retained secundines.

Excluding cases of endogenous infection, febrile abortion under three months gestation is undoubtedly self or criminally induced. If, during the waiting period, the abortion has not completed itself, evacuation is indicated, the method used depending upon the amount of cervical dilatation and the month of gestation. In febrile cases with severe hemorrhage, immediate evacuation should be performed and the uterus should not be packed, if bleeding seems to be controlled.

The essentials in the treatment of incomplete afebrile abortion are: (1) ice bag to lower abdomen; (2) quinine not exceeding 15 gr.; (3) pituitary extract 5 units every six hours or fluidextract of ergot 10 minims t.i.d. for three days, to be repeated if bleeding recurs or incompleteness is suspected (the equivalent may be given in ergotrate, i.e., half of a 5 mg. tablet t.i.d. for a maximum of three days); (4) 1000 c.c. of 5 to 10 per cent glucose solution in normal saline, in emergency, for shock, profuse blood loss, or in septic cases with reduced food intake; (5) blood transfusion, 500 c.c., as indicated.

In febrile cases the following are added: (6) sulfanilamide. If intra-uterine or blood culture is not practical it may, nevertheless, be advisable to give the drug in tablet form, 15 gr. every four hours the first day, 10 gr. every four hours for the second and third days, after which, the concentration is maintained at 10 mg. per 100 c.c. of blood. If this determination is not available, give 40 gr. on subsequent days up to five to seven days. Discontinue for a few days and repeat if lack of improvement warrants. A rise in temperature and cyanosis may occur, but they are not important; Nausea of varying degree may necessitate subcutaneous administration which is given immediately and slowly by drop method in the anterior thigh. This solution is prepared by dissolving 0.8 Gm. of the drug in 100 c.c. of boiling normal saline solution which is then cooled to body temperature. It deteriorates on standing.

Five grains of sodium bicarbonate is given with each oral does to limit the nausea and prevent acidosis. No other drug is administered, especially not sulfates, during treatment and for three days after treatment is discontinued. Hemoglobin, leucocyte and red cell counts are taken before treatment and daily after treatment. Hemolytic streptococcus infection accentuates the depreciation of the blood. Low values in a kidney function test contraindicate this treatment. Urinalysis should be done daily. Blood in the urine indicates cessation of treatment. The drug is stopped if acute hemolytic anemia, leucopenia or sulfhemoglobinemia develops. A transfusion

is given before treatment if hemoglobin is below 70 per cent (Sahli). Preliminary blood grouping is desirable. If anemia alone develops and can be controlled by transfusion, treatment may be continued. In the absence of the more complicated laboratory procedures, one will have to depend upon objective and subjective signs and prophylactic transfusion.

Chemotherapy has been limited to the use of sulfanilamide which has selective action and has been used successfully in gonococcus, staphylococcus, hemolytic streptococcus and *Clostridium Welchii* infections. The last two are usually fatal, especially if blood culture is positive. However, there have been miraculous cures, particularly when the infection is unmixed and treatment is instituted early. The dangers from sulfanilamide are minimal if proper precautions are taken. If it is not tolerated by mouth, parenteral administration is indicated.

Transfusion is very valuable in small amounts frequently given (200 to 300 c.c.).

Surgery. The retained products are not evacuated until at least five days of normal temperature have elapsed. The only exceptions to immediate evacuation in febrile cases are: (*a*) severe or prolonged profuse hemorrhage; (*b*) dilated cervix, filled with decidua, preventing drainage. In the first case evacuation should be complete, with packing for twenty-four hours, if necessary, to control bleeding.

Fever may be due to sapremia rather than infection; the chills and temperature will return, immediately, to normal. Clinically, the patient's appearance does not seem to justify diagnosis of infected abortion.

A pelvic abscess in the cul-de-sac may be emptied by posterior colpotomy. Posterior parametritis may be mistaken for an abscess. Incision is useless and dangerous. An intraligamentous abscess may be drained, when it rises above the pubis, by incision parallel to Poupart's ligament.

Of our 1,000 cases, 26 per cent were febrile. All were treated conservatively, giving a mortality of 1.9 per cent or a corrected mortality of 1.3 per cent, if the patients entering the hospital moribund are eliminated. Expectant-active treatment is justified by the lower mortality, fewer disabling sequelae and the recognition of established surgical principles. The temperature reaction of pelvic examination indicates the disruption of the leucocytic barrier; invading the uterus at the improper time often determines a fatal issue, as many a consultation recalls.

Missed Abortion. Taussig estimates that one-tenth of the spontaneous are missed abortions. Litzenberg recommends evacuation as soon as the diagnosis is made. Quinine and pituitary extract, after sensitization of the uterus with repeated doses of 20,000 units of estrin, may cause proper uterine contractions. Failing in this, the cervix may be softened by packing and in advanced cases, the bag, in early cases, graduated dilators, will open the womb. Then evacuation is carried out with ovum or sponge forceps, followed by packing for the usually free hemorrhage.

Habitual Abortion. Evidence is available that habitual abortion, in the absence of general disease or local pathology, is due to a disturbance of estrogen production and the prolan-progesterone mechanism of pregnancy. The values of these, in blood and urine, vary at different periods of gestation and although the minimal requirements for successful continuance of pregnancy are as yet not definitely known, the new treatment of threatened and habitual abortion seems to show results.

Endocrine assays by Brown, Hendry and Venning in twenty-five cases of habitual abortion indicate that alternate daily doses of less than 5 mg. or 5 rabbit units of progesterone are not likely to have much effect. Abortion is most likely to occur at the time the necessary gestational hormones are transferred from production in the ovary to the placenta. Since this period is variable and assay is not within the province of many, at least 5 mg. of progesterone should be given daily or on alter-

nate days, with increased dosage in cases of threatened abortion. Administration should begin a few weeks before the time of the previous earliest abortion. If abortions in the individual have occurred early and late, the treatment may be interrupted in a portion of the interval.

The well known responsibility of hypothyroidism in sterility suggests the use of thyroid extract in habitual abortion, with dosage determined by symptoms and basal rate.

An additional probable factor in habitual abortion, vitamin E deficiency, can be provided for in the form of wheat germ oil, 3 to 6 c.c. daily in capsules of 1 c.c. each.

Technique of Abortion. The methods used at the Minneapolis General Hospital are as follows:

1. If dilatation is necessary, graduated dilators are used, in the early months, a Vorhees bag in the later months. A long and firm cervix is not easily dilatable; a gauze pack for twelve to twenty-four hours will soften it sufficiently to insure dilatation with a bag.

2. Up to the fourth month, evacuation is performed with ovum or sponge forceps after determination of the position of the uterus and the length of the cavity. Measurement is done with the same instrument, which because of its blunt extremity, is not likely to perforate the uterus.

After the third month, one or two fingers are used to separate the placenta, at the same time pressing the uterine wall to the fingers from above. Precede this procedure with 1 c.c. of pituitrin hypodermically.

3. The curette, a blunt one, is used only in cases of long standing with fairly firm fundus.

4. Packing is usually unnecessary and is to be avoided except for hemorrhage; however, it is nearly always necessary after evacuating a missed abortion.

SUMMARY

1. Treatment is given for various types of abortion except therapeutic.

2. Recent advances in treatment comprise the use of sulfanilamide in certain infected cases. Vitamin E and progesterone are administered in threatened and habitual abortion.

3. Conservative treatment is stressed.

4. Technique of operative procedures is indicated.

THE HEMORRHAGES OF LATE PREGNANCY AND LABOR: PLACENTA PREVIA AND ABLATIO PLACENTAE

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INTRODUCTION

IT is indeed fortunate that placenta previa and premature detachment of the placenta are such infrequent complications of the puerperal state, for, while they severally occur but once in 500 advanced gestational periods the resultant deaths constitute approximately 7 to 10 per cent of all puerperal deaths. The lethal dangers being so great, it behooves all obstetric attendants to become thoroughly conversant with every diagnostic detail of these two emergencies, so that prompt and appropriate therapy may be instituted. It is imperative that the attendants be facile in combating these catastrophies, or possess the moral courage to transfer the responsibility to someone so qualified.

Placenta previa and ablatio placentae have a number of attributes in common, as well as some which are vividly dissimilar. Their convergent details lead to diagnostic uncertainty, even confusion; their diversities are so dramatically distinctive that he who runs may read.

History. The tracing of the development of the knowledge of the one may not be dissociated from the other, for both have a common origin and course. The Hippocratic teaching that nature had so generously provided a nesting place in the fundus of the uterus that invariably the placenta was there attached was considered gospel long over a millenium and a half. During all this time it was held that the hemorrhage of advanced pregnancy was due to a fundal separation, placental prolapse, and possible birth before the egress of the child. Even when the refutations of keen observers of the early sixteenth to eighteenth century became known, many still believed that Hippocrates was right and even when the truth did prevail many vehemently maintained that the normally situated placenta could not separate in pregnancy.

Paul Portal (1664) graphically described placental presentations but no credence was accorded to the new teaching. Gottlieb Schacker (1709) ably reported the postmortem findings in a woman dying from a premature placental detachment where the uterus was filled with blood. Bernard Albinus (about 1750) recorded a similar example which he discovered by autopsy. Giffard (1734), Smellie (1766), Levret (1766) added certain basic principles to our knowledge of placenta previa. Rigby (1776) first gave a clear clinical and anatomic differentiation of placenta previa from premature detachment. We may doubt the accuracy of some of his diagnoses, but we must concede that he did see clearly the segregation of hemorrhages into the two definite types. He denominated a placental presentation as *unavoidable*, and the other as *accidental.*

A. C. Baudelocque (1804), in his thesis on uterine hemorrhages, lucidly described cases of placental detachment wherein the uterus was distended with blood. Mme. Boivin, in discussing his presentation, denied the possibility of such occurrences as he described, for neither she nor Mme. La Chapelle had seen such in over 42,000 labors. Hodge of Philadelphia took the stand of Mme. Boivin. As late as the last decade of the past century Lusk and Cazeaux and Tarnier dismissed the subject with scant paragraphs.

Tanner (1851) presented a paper based upon a few cases culled from the literature; Hicks (1860), Goodell (1870), and H. R. Storer (1892) supplemented these, until the last had some 140 cases assembled. The

writer (1901) collected 198 cases not previously compiled with two reports of original cases in a paper entitled "Ablatio Placentae." Up to this time, while certain British hospitals, notably the Rotunda of Dublin, annually included cases of accidental hemorrhages in their statistical reports, comparable in number to that obtaining for previa, numbers of large American hospitals with large obstetric services failed to record a single instance. To this day, most of the federal and state vital statistics concerned with puerperal mortalities enter the deaths from premature detachment among "other puerperal hemorrhages," though they are almost as numerous as deaths from placenta previa.

Etiologic Resemblance. It is generally believed that endometritis is a fruitful contributory factor in the preparation of the lower uterine segment for a previal implantation. Premature detachment has been accorded the same etiologic influence, either as a contributory or direct association.

Source of the Hemorrhage. The two entities have a common origin for the bleeding—from the opening of uterine sinuses; in one the blood losses result from a separation of a viciously inserted placenta, in the other, from a normally implanted one. The hemorrhage in both *may* be initiated by some casualty. The hemorrhage in frank previas is almost invariably "silent." Almost never is the pain or discomfort intrinsic to the condition. The bleeding in premature detachment, on the other hand, produces an array of objective and subjective signs which vary with the placental location, the suddenness and extent of placental separation, and the amount and the rapidity with which the effused blood accumulates within the uterus. The line of demarcation between a high lateral previa and a low normally implanted placenta may not be clinically demonstrable: the lower rim of the respective types may become detached, and the escaping blood may arouse no symptom, or if the extravasated blood be restrained for a period, there may be vague to marked subjective disturbance.

Nomenclature. The terms placenta previa, placental presentation, and unavoidable hemorrhage are so lucid they carry no false or ambiguous interpretations. However, the titles adopted for premature detachment of the normally situated placenta mostly connate erroneous concepts of the etiology, or of the symptomatology. Accidental hemorrhage carries the implication of a mishap or traumatism, and the majority of the writers previous to the dawn of this century accepted the name as such, although Rigby was most emphatic that he meant the term to cover fortuitous circumstances. The old literature teems with case reports wherein overt or specious traumatisms were the cause—and when these were not pronounced or occurring imminently in relation to the hemorrhage, the attendants avidly sought, and found, some sort of jolt long antedating the catastrope which was duly assigned as the "cause." A. C. Baudelocque (1804) associated the word "concealed" with Rigby's "accidental"—still further befogging the title. Very few cases are reported where from the moment of occurrence to the time of delivery there is no external evidence of blood loss, since sooner or later patent hemorrhage will supervene. *An overt hemorrhage is never a concealed one.*

That the atmosphere might be clarified, the author sought counsel from a professor of Latin and Greek, explaining the picture of premature detachment: He asserted that the analogy of ablatio retinae justified the name ablatio placentae or placenta ablata—the placenta is torn away. Therefore, the writer has used this term as the generic description for premature placental separations, due to any cause.

De Lee (1901) suggested that the condition should be christened abruptio placentae, but abruptio is incorrect in its premises as not more than one detachment in ten has a sudden, violent or tumultuous onset. The term thus carries erroneous implications of the symptomatology. The

title of this paper, *Hemorrhages in Late Pregnancy and Labor*, is misleading in an anatomic and chronologic sense, as both placenta previa and ablatio may be the cause or the comitant of early abortions or miscarriages.

PLACENTA PREVIA

A previa obtains when any portion of the placenta, large or small, dips into or below the potential site of the retraction ring. This means that part of the placenta is implanted in the lower uterine segment or the dilating part of the uterus. It is unfortunate but true that obstetricians have not agreed upon a common grouping of the degrees of placental presentations, or upon a conception of what the designating names imply, or upon the anatomic conditions which must exist for the diagnosis of the extent of placental presentation. According to the caprice of the individual writer two or more of these terms are employed—central, complete, incomplete, partial, marginal, and lateral.

The degree of the previa is interpreted at the time of the diagnostic examination, whether the os be undilated or widely opened. However, it should be determined by the correlation of the placenta to its site before any effacement or dilatation has occurred. Thus the attendant, when belatedly examining the patient, should endeavor to envisage conditions as they were originally, not as he finds them. Effacement and passive dilatation are present in nearly all women as labor is imminent. When there is a placental presentation, effacement produces new relations of the placenta and its site which may be accomplished only by a tearing of their juncture. The hemorrhage is merely the manifestation of the placental separation. As dilatation advances, the placenta is separated and assumes new relations to the structures upon which it had been implanted. This being true, a complete presentation, when the internal os has been materially opened, will appear to be an incomplete or partial type; the marginal form will be evidenced as a partial or incomplete previa; and the lateral may have the placental periphery quite at the internal os. The placental rim which juts into the area of the undilated os has no clinical significance over the marginal form, so the word partial may with propriety be discarded.

These fundamental precepts lead us to believe that the following three types of previa cover every situation—lateral, marginal and complete—the type being visualized before effacement has taken place.

FREQUENCY

Almost all pronouncements of the incidence rates of placenta previa (in fact, all obstetric phenomena) are based upon the experiences of individuals with special opportunities, or the numbers housed in their respective hospitals. Such figures are fallacious in that they do not reflect the prevalences of the anomalies in large aggregations of population. In the case of previa, the numbers which are coincident to abortions and miscarriage are never included as they are unavailable. Hospitals of necessity have a considerable preponderence of pathologic cases over other institutions which cater to a private clientele.

The Committee on Prenatal and Maternal Care of the White House Conference sent questionnaires to some 600 hospitals of the United States requesting a résumé of their obstetric statistics for 1929. No hospital was circularized which had not shown more than 100 births in a previous issue of the hospital number of the *Journal of the American Medical Association*. Of the 489 institutions which responded, 284 gave the numbers of previas attended by their physicians. These hospitals had obstetric capacities from 5 to 123 bassinets, and annual births from 97 to 3,228. In all, 1,024 cases of placenta previa occurred in this group. The average number of previas for each hospital was 3.9 cases. (Table 1.)

When we consider that a large proportion of our hospitals have almost as many obstetricians on the staff—let alone the numbers of "courtesy" members—as there are obstetric beds, we perceive the grave problem in giving physicians adequate training and adequate opportunities to develop experience. As nearly all computations of obstetric anomalies are based on hospital experience, they do not reflect true incidences. Until all lethal obstetric anomalies and their demises are nationally recorded we must accept a figure of not more than one placenta previa in 500 advanced pregnancies.

TABLE I
FREQUENCY OF PLACENTA PREVIA

Authority or No. of Hospitals	No. of Births	Total Births	No. Placenta Previa	Average No. per Hospital	Incidence	Ratio of Previa to Births
284*	97 to 3,228	151,857	1,024	3.6	0.67	1: 148.3
45*	97 to 200	6,852	111	2.5	1.62	1: 61.7
35*	1,001 to 3,228	51,399	276	7.9	0.54	1: 186.2
1	97	97	4	4.0	4.12	1: 24.3
1*	115	115	5	5.0	4.35	1: 23.0
1	176	176	7	7.0	3.98	1: 25.1
1	447	447	13	13.0	2.90	1: 34.4
1	1,012	1,012	1	1.0	0.09	1: 1,012.0
1*	1,313	1,313	1	1.0	0.08	1: 1,313.0
1	2,174	1,214	1	1.0	0.05	1: 2,174.0
D. Findley	.....	3,464,278§	21,706	....	0.63	1: 159.6
Müller†...	.....	876,432	813	....	0.09	1: 1,038.0
Schwarz‡..	.....	519,328	332	....	0.06	1: 1,564.0

The enormous variations of incidence in different hospitals permit of but one deduction—the hospital statistics offer no clue as to the actual frequency in a large population—the only true basis for computation. Probably the actual ratio is between 1: 500 or even 1: 1,000.

* From White House Questionnaire.
† Mass statistics for the States of Oberhessen-Würtemberg.
‡ Mass Statistics for the State of Oberhessen.
§ Estimated from data given.

ETIOLOGY

Contributory Causes. It is quite generally believed that endometrial inflammatory alterations prior to pregnancy contribute directly or indirectly to the nidation of the ovum in the lower segment, but this belief is purely apocryphal. It is undoubtedly true that women who have borne children are more likely to have been exposed to infections as the result of operations, abortions or puerperiums than the woman in her first pregnancy. Multiparity is assumed to be a predisposing cause to the formation of a previa. Of eighteen previas in the Rotunda Maternity only one was in a primiparous woman. From the time of Rigby this has been noted; Smellie, Gifford and Rigby found that of fifty-one previas all but three were multiparae. Doranth reported 316 previas with sixty-three present in primiparae—19.9 per cent. It is evident that multiparity does have some peculiar influence on the production of previa.

Age, too, has been given as an important predisposition to the formation of a previa. The value of the statement is somewhat negated in that one-third or one-fourth of all children are borne by women under 25. However, if endometritis, parity and age were potent contributory causes we would see frequent recurrences in the same woman. Yet a repetition of the complication is rare, and recurrence in three or more pregnancies is unique.

The writer is convinced that endometritis, multiparity and increasing years are interesting data for speculation, but are basically sequences of some unknown factor; he is strongly of the mind that future investigators will uncover a biologic reason for nature's selection of multigravidae for the ravages of previa. The influence of the endocrines upon every phase of reproduction—sterility, fecundity, development of the ovum, and changes in the endometrium—has been clearly proved. The aberrant influence is transitory, affecting the single nidation. Herein is a reasonable postulate for the contributory or even direct cause of placenta previa.

Direct Causes. Except for one explanation the putative direct causes are in the same realm as the contributory influences. Gravity was long held to be a cause, but whether the woman be erect, prone or supine the uterine axis is never long in the perpendicular, and its flexions militate against the theory. It is more tenable to believe that the ovum, bathed in the uterine secretions, is impelled downward by

ciliary motion and muscular activity. The decidual reaction may be delayed, so that only when the egg reaches the lower segment has the process been developed sufficiently for nidation. Possibly the fertilized ovum has not fully ripened and reaches maturity only when it comes in contact with the mucosa of the lower segment. As we know little of the physiologic reasons for implantation of the ovum above the retraction ring, we have no concrete explanation for its nesting below that area. It is an interesting actuality that a pure fundal attachment of the placenta is second in frequency to its location in the lower segment. Vascularity must bear an important part in paving the way for nidation.

Reflexal Placenta. Hofmeier and Kaltenbach (1888) offered a specific explanation for the production of a previa which was elicited by the study of decidual casts. They found early abortion specimens where the decidua reflexa had not yet coalesced to the vera. Cotyledons had sufficiently hypertrophied to be positively evident, some being attached to the vera while others were developing in the reflexa. The specimens clearly showed that the reflexal cotyledons were directed towards, and were near, the lower pole of the decidual cast. The accurate deduction was made that the reflexal cotyledons shortly would become adherent to the decidua vera in the lower segment, producing a previa.

Various authorities studied their specimens of decidual casts, and found repeated corroborative evidence of the truth of the assertions of Hofmeier and Kaltenbach. The growth of the reflexal placenta elucidates the method of the placenta's bridging the internal os. Noone has declared that this is the only method by which a placenta may develop as a previa, but others have maintained that it is but one method of production. Nearly all agree that the maturing placenta may reach and cross a tightly closed internal os without a reflexal origin.

A large placenta has been declared to be a cause of a previal placenta, especially as the placental disc is quite commonly larger than normal. The large placentae of multiple pregnancies would clearly substantiate the allegation that large placentae are an element in that twins occur with twice the frequency in previa as they do normally. Some consider that the large thin placenta of previa is nature's endeavor to obtain adequate blood supply for the growing ovum. A placenta succenturiata may be present with either the parent body or one of the accessory parts presenting.

SYMPTOMS

Placenta previa has but one symptom—hemorrhage. The bleeding usually occurs without pain or even discomfort. If pain is present, it is almost invariably extrinsic to the previa, except in those instances where the placenta barely dips into the lower segment, and the escaping blood is retained for a brief period. The first bleeding may occur at any moment after nidation has occurred, and the maturing cotyledons show the first appearance of the future placenta. Before the fourth month the gestational interruptions have the distinctive features of an abortion or miscarriage, whether the previa is the cause or merely coincident. These early ovular expulsions due to previa are rarely reported, owing to remissness in studying the specimens. The infrequent reports do not imply an immunity to placental separation in the first trimester. The relative paucity of cases reported between the fourth and seventh months suggest that this is period of quiescence. It is credible to hold that in these months the placenta is in full maturity and secure against separation, while after the second trimester the progressive senility of the placenta may contribute to the readiness of the uteroplacental union to be severed under adequate stimuli.

David Findley reported that in 4,416 previas, 3,763 (84.98 per cent) patients had the first hemorrhage after the thirty-first week. According to the report of the Children's Bureau on Maternal Mortality in Fifteen States, 408 deaths from previa

were reported, of which 288 were recorded when the first hemorrhage took place: before the thirteenth week, seven (2.4 per cent); from the thirteenth week to the twenty-fifth, inclusive, thirty-one (10.7 per cent); from the twenty-sixth week to the thirty-ninth, inclusive, 201 (69.1 per cent); in the fortieth week, forty-nine (17.0 per cent). About 10 per cent of previas have the first hemorrhage when labor takes place.

The first hemorrhage was slight in 14 per cent, moderate in 26 per cent, and profuse in 60 per cent.

Bleeding may come on spontaneously, as the direct result of painless contractions, or because of the changing relations of the placenta at the beginning of retraction of the lower segment. It may appear during sleep, or in a quiescent period of wakefulness: the hemorrhage may be precipitated by coitus, may follow a local examination, or may result from blows, falls, or from other casualties, large or small. The amount of blood loss may be in direct proportion to the placental separation, or a large sinus may be exposed from a minimal disruption, resulting in an alarming hemorrhage.

DIAGNOSIS

Recognition of a previa may be obtained only by physical examination. Abnormal positions and presentations may cause a deviation of contour of the uterus and abdomen; their presence is corroborated by palpation. Abnormal fetal lies result from the presence of the placenta at the pelvic brim, which compels the head to take an eccentric position, and thus the development of transverse and breech presentations is favored. While these deviations of fetal position are common in previa, any pathology which disturbs the contour of the pelvic brim tends to produce the same effect. The deviations in position are presumptive evidences in the presence of bleeding during the last trimester, but prior to that time they are distinctly physiologic. Auscultation will corroborate the abnormality of position if marked, and will give indispensable knowledge of the fetal condition if it is in jeopardy or is dead. If the placenta is situated anteriorly, auscultation may permit a detection of the bruit suprapubically. Müller reported that in 1,418 cases of previa, transverse presentations were found in 272 (23.8 per cent and breech in 107 (9.3 per cent).

Conclusive evidence of the presence of a previa may be derived from a vaginal or rectal examination, even before there is other suspicion of its existence. Routine local examinations between the fifth month and term would permit a diagnosis in all cases where there is a frank placental presentation, but the dangers of inducing a hemorrhage in the office from such examinations is ever present. The trite behest that a vaginal examination should be made at the time of the pregnant woman's first visit, and later only on some definite indication, has obtained these many years. However, one must determine whether it it is preferable to give repeated, routine, local examinations as part of maternal care in order to isolate the rare woman with a previa, or to await the signal flare of hemorrhage before undertaking an examination. Which is the lesser of two evils?

The vaginal examination must be conducted under the strictest aseptic technique. Except under direct necessity it should be the rule that no vaginal examinations should be made unless all the paraphernalia requisite for immediate arrest of bleeding and all measures for terminating pregnancy are at hand. It is highly recommended to have the woman transported to the hospital, in an ambulance if one is available. On arrival she should be prepared for immediate delivery, the operating room set up for the emergency, and then only, under an anesthetic, should the parturient canal be entered. Exceptions to this dictum are few, for makeshift examinations are fraught with especial perils. Trained fingers elicit practically as much by rectal examinations as may be obtained through the vagina, and this does not carry risk of infection. Rou-

tine practice only is required to acquire proficiency.

The vaginal wall is commonly relaxed, and often cyanotic. The cervix is soft and relaxed, and usually the canal is dilated to some extent. In the area of the placental site there is an increased pulsation due to the undue vascularity of the tissues. In lateral and marginal types the cushion of placenta is found interposed between the finger and the presenting part, while on the opposite side the fetal part is more readily perceived. In a complete previa the fetus may not be felt at all, or only indefinitely.

It is usually possible to determine the existence of the previa without entering the cervical canal, but when this procedure is necessary it must be carried out with the utmost gentleness. The placenta alone is felt if there is a complete previa. If the placenta is marginal, the placental rim is easily palpated. In lateral forms the finger mounts a variable distance before the placental border is reached. The membranes, when palpable, are often thickened and the surface rough, due to the presence of thickened chorionic laeve and shreds of decidua where the sac has been stripped from its adhesions. The palpation of the placenta alone is proof positive.

Roentgen Examinations. Two methods have been suggested: (1) opaque dyes injected into the amniotic sac; (2) instillation of soluble dyes into the bladder. The former method is hardly worthy of consideration as the risks are too great, and, with our present knowledge, more accurate information may be obtained by more conservative methods. Cystography depends upon the fact that the placenta will raise the head above the normal station; to be suggestive there should be at least 1 cm. between the shadows of the opaque bladder and the fetal head. However, the contracted pelvis produces the same effect, or even a prolapsed ovary, kidney, etc., before the head.

Beck and Light made cystographic studies of 90 patients with vaginal bleeding. In the breech or transverse presentations (nineteen cases) there was an error of over 20 per cent. In the seventy-one vertex positions there were eight errors and in seventeen true previas there were four conclusive results. Jablonski and Meisels believe the method is of value, though if there is a posterior location of the placenta it may be overlooked. Robecchi and Zocchi are of the opinion that the method is only of value after the seventh month; before that time the immature ossification of the fetal skull and its high station preclude all positive information. They further believe that there may be no differentiation of a previa from a severe ablatio placentae.

Under the circumstances these procedures should not be recommended for general use. Further progress in the hands of expert roentgenologists and obstetricians should be made before we may accept the methods as of any value. A timely vaginal or rectal examination will give conclusive information.

DIFFERENTIAL DIAGNOSIS

This phase of the subject will be discussed in the section on ablatio.

CLINICAL COURSE

The hemorrhages of placenta previa may manifest themselves at any period of gestation, from the earliest time until the onset of labor. The first hemorrhage is often slight, but may be profuse or fulminating. The bleeding may be a continuous dribble, or a protracted interval may elapse before the next bleeding recurs. Some few lateral and marginal previas have the first bleeding only in labor, but rarely does a complete previa manifest itself so late. However, instances have been recorded where the placenta, entirely separated, was expelled before the fetus, with slight risk to the mother. The medical attendant never should countenance such an unusual course. Spontaneous labor may occur in certain minor placental presentations, and here success is dependent upon the prompt descent of breech or head which will compress the bleeding area.

PROGNOSIS

Maternal. The outcome for the mother afflicted with a previa is influenced by numerous circumstances. Her physical condition contributes to success or failure. The degree of previal presentation is of vital import as the maternal risks increase in proportion to the type from the high lateral to the complete forms. The amount of blood lost is of marked significance and the speed with which it may be arrested is a paramount issue. Promptness in augmenting blood volume, and celerity in blood transfusion are vital. A sudden violent blood loss is more serious than the same amount slowly escaping.

Lack of respect for minor bleedings in a pregnant woman may spell disaster; procrastination in the presence of any vaginal bleeding is unpardonable. It is stated in the report of the Children's Bureau (publication #223) that of 236 women dying of previa who had had a warning hemorrhage, only eighteen had received prompt treatment.

He who employs polypragmatic policies will have the maximum of disaster, especially if he performs cesarean sections routinely. Disaster awaits the surgeon who attempts a cesarean after others have futilely attempted a vaginal delivery. The conditions pro and con in each case must be weighed, and that operation selected which will give the maximum of success. One must appreciate that heroic surgery is not suitable to all cases of placenta previa. The best method is that which requires the minimal operative detail. Manual dilatation of the cervix, version, and rapid extraction form a trio of reprehensible obstetric practices.

Hemorrhage has a reciprocal reaction with anemia: the former creates the latter and the latter perpetuates the former by producing uterine atony and lowering the coagulability of the blood. Anemia makes the patient peculiarly vulnerable to the ravages of sepsis. When a previal patient dies from sepsis, the infection need not necessarily have been introduced from without; often it is autogenous, the result of activation of the vaginal flora. The prolonged retention of the bag or tampon, the repeated vaginal manipulations tend to activate the bacteria. The blood in the vagina offers an ideal culture medium and the body heat provides the appropriate temperature. The proximity of the placental site to the potentially active germs, the exposure of abrasions to the purulence of the lochia all contribute to an autogenous infection.

Read (1861) and Müller (1877) presented figures which demonstrated the dangers of sepsis. The former recorded 229 previal deaths, of which thirty-eight (16.5 per cent) resulted from sepsis. The latter stated that, of the 212 deaths in his series, fifty-four (25.4 per cent) followed sepsis. Irving (1936) showed that, of twenty-two previal deaths, four (18.1 per cent) were due to the same cause.

The emergency obstetric service of large institutions necessarily must admit their quota of possibly or actually infected women. A full 50 per cent of all previal deaths result from ante- or intrapartal hemorrhage; a quarter of the patients succumb from a continuation of the hemorrhage into the third stage; the final group of deaths results from sepsis or some concurrent disease.

Since accouchement forcé has been repudiated, the dangers of postpartum hemorrhage or hemorrhage from lacerations have been greatly curtailed. Asepsis and sane conservatism have reduced the gross maternal mortality by 60 or 70 per cent, but sepsis continues to hold the same ratio to hemorrhage as the cause of a lethal result as before the antiseptic era. Table II shows the comparative results in various periods since 1860. To obviate confusion, lateral, marginal and partial placenta previas have been combined under the caption of "incomplete." Table IV presents the mortalities as influenced by treatment.

Fetal. The life of the fetus in utero is precarious even when its maternal environment is ideal. From the time of conception

until birth the fetus wages a losing fight and the fortuities of early neonatal life carry a heavy toll even under normal or average computations. When previa exists has rigid indices. Statistics indicate not better obstetrics, but that in later periods the time of fair viability has been advanced.

TABLE II

MATERNAL MORTALITY RATES IN PLACENTA PREVIA (COMPLETE AND INPCOMLETE*) IN DIFFERENT PERIODS

Authority	Total Cases				Complete			Incomplete*		
	Number	Died	Per Cent	Per Cent Septic Deaths	Number	Died	Per Cent	Number	Died	Per Cent
Read† (1861)	1,024	229	22.2	16.5	347	99	28.5	225	36	16.0
Müller† (1877)	953	237	24.8	25.4	345	109	31.6	394	57	14.5
Holmes† (1905)	2,756	213	7.4	....	350	47	13.4	1,022	44	4.3
Holmes† 10 reports from above	1,011	31	3.1	....	134	8	6.0	437	11	2.5
Holmes (1929) 256 Hospitals‡	1,005	86	8.6							
D. Findley (1937)	7,425	426	5.7	....	2,063	220	10.7	5,362	206	3.8
Irving (1937)	308	22	7.1	18.3	77	11	14.3	231	11	4.8

Modified from Davis' "Gynecology and Obstetrics."
* "Incomplete" includes lateral, marginal, partial.
† Cesarean sections not reported in these groups.
‡ Data derived from questionnaire of the White House Conference.

TABLE III

FETAL MORTALITY RATES IN PLACENTA PREVIA (COMPLETE AND INCOMPLETE*) IN DIFFERENT PERIODS†

Authority	Total Cases			Complete			Incomplete*		
	Number	Died	Per Cent	Number	Died	Per Cent	Number	Died	Per Cent
Read§ (1861)	1,031	526	51.0	302	197	64.9	207	122	58.9
Müller§	2,365	1,518	64.2	320	223	69.6	382	182	47.6
Holmes§ (1905)	1,985	1,075	54.1	216	174	80.5	538	272	50.6
Holmes§ (9 reports from above)	381	147	38.9						
Holmes (1929) 158 Hospitals‡	636	246	38.7						
D. Findley (1937)	7,402	2,412	32.6	2,040	806	39.5	5,362	1,606	29.9

* Incomplete includes lateral, marginal, partial.
† Modified from Davis' "Gynecology and Obstetrics."
‡ Data derived from questionnaire of the White House Conference.
§ Cesarean sections not reported in these groups.

every phase of fetal life is rendered tenfold more hazardous. The first hazard arises from the prematurity of the interruption of pregnancy. Unfortunately there is no generally accepted standard as to what constitutes prematurity; comparative statistics will be valuable when *prematurity*

Read (1860) and Müller (1877) considered that pregnancy was interrupted by placenta previa in 65.6 and 55.3 per cent respectively, their criterion of prematurity being after the twenty-eighth or thirtieth weeks. D. Findley (1937) found that 15.02 per cent of the pregnancies were terminated

prior to the thirty-first week; i.e., in 4,416 previas, 663 babies were born before that period. Irving (1937), at the Boston Lying-in Hospital, reports that of the 315 infants 116 (37 per cent) were born before the thirty-fifth week. Of the 315 babies, seventy-one (24.9 per cent) weighed less than 4 pounds. The fetus is also destroyed by the placental separation in pregnancy or labor. Irving states that forty-eight (15.2 per cent) were dead when the mother was admitted.

to mother and fetus it should ever be kept in mind. Cesarean section relieves the fetus of the stresses of birth, and the fetal results vie with those following spontaneous birth, with or without an artificial rupture of the membranes. The neonatal existence is beset with peculiar hazards since prematurity and impaired condition following birth render the infant particularly vulnerable to the maladies of the newborn.

Kuhn had forty-three previas in private practice—at the end of two months only

TABLE IV

MORTALITY OF PLACENTA PREVIA AS INFLUENCED BY THERAPEUSIS*

Therapeutic Methods	Maternal Mortality				Fetal Mortality		
	Number	Died	Per Cent	Per Cent Morbidity	Number	Died	Per Cent
Ruptured membrane†	2,070	37	1.8	4.8	1,958	436	22.2
Spontaneous birth†	3,068	70	2.3	4.8	2,244	525	23.4
Hydrostatic dilators	4,464	263	5.9	16.2	3,113	1,542	49.5
Hicks' version	10,660	686	6.4	23.2	8,213	5,523	67.2
Cesarean section	5,166	337	6.5	40.3	2,154	533	24.7
Vaginal tamponade	477	32	6.7	....	475	239	50.3
Accouchement forcé	291	71	24.4	22.6	282	133	47.2
Totals	26,196	1,496	5.7	....	18,439	8,931	48.4
Findley's grand total	47,828	3,454	7.2	....	27,047	14,427	53.4

* Adapted from Findley's analysis of 47,828 cases, with relative morbidity rates as reported by Irving. Modified from Davis' "Gynecology and Obstetrics."

† Dr. Irving rightly considers these two together as expectant treatment.

The causes of death in previa are (1) asphyxiation (directly due to placental separation or due to the placental compression in birth, cutting off aeration of the blood), and (2) hemorrhage from the lacerated placental tissues. Blood counts on live infants and on dead ones born before coagulation has set in will clarify this postulate. If fetal death is due to acute anemia, a timely blood transfusion might save some.

Finally, the type of intervention has an enormous influence on the life expectancy of the fetus, just as is the case with the mother. The simpler the intervention the lower the gross fetal mortality; the more drastic the operation, the greater will be the fetal loss. As this dictum applies equally

two infants remained alive. It is an interesting sidelight that in the 47,828 previas collected by Findley the status of the baby after birth was mentioned in only 27,074 (56 per cent). That no mention of the outcome of the fetus was given in 44 per cent illustrates the scant regard too many reporters grant the fruit of the pregnancy. The fetal mortality rates are presented in Tables III and IV.

TREATMENT

General Considerations. Two imperative demands exist in the therapy of placenta previa: the first is that bleeding shall be arrested at the earliest possible moment, and that there shall not be recurrences; the second that measures shall be taken which

will eventuate in the termination of labor. The first is accomplished by two expedients which are the precursors of the second, the tampon (ordinarily an abomination) and the hystereurynter serve this purpose. Hicks' version is valuable in both spheres. The great advantage in these three is that during the period of waiting active measures may be taken to combat the ills of the anemia, and to provide supportive treatment.

cesarean section who are tainted with a possible infection, who are in a distressing condition from shock and hemorrhage, or, ordinarily, whose fetus is dead or in such a precarious state that there is no reasonable expectation it will survive the ordeal of the operation. Such circumstances belie the putative advantages of section, and in these cases another type of delivery is chosen to absorb the evils and dire consequences.

TABLE V

COMPARATIVE FREQUENCY OF ABLATIO PLACENTAE AND PLACENTA PREVIA FROM THE SAME SOURCES

Authority	No. of Births	Ablatio Placentae			Placenta Previa		
		No.	Incidence	Percentage	No.	Incidence	Percentage
Churchill	68,982	85	1:811	0.12	171	1: 403	0.25
Smyly	61,453	70	1:877	0.11	41	1:1499	0.06
Irving*	34,392	353	1: 97	1.03			
Irving*	28,391	.....	.....	....	308	1: 111	1.08
Solomons	2,376	29	1: 82	1.22	18	1: 132	0.75
N. Y. Lying-in Hospital, 1934	2,637	9	1:293	0.34	13	1: 203	0.49
N. Y. Lying-in Hospital, 1937	2,732	13	1:201	0.45	15	1: 182	0.55
N. Y. Lying-in Hospital, 1938	2,923	8	1:365	0.27	19	1: 154	0.65
Chicago Lying-in Hospital, 1925–1927	6,097	48	1:127	0.78	48	1: 127	0.78
Holmes, 123 Hospitals W. H. C., 1929	100,016	555	1:180	0.55			
Holmes, 284 Hospitals	151,857	.....	.....	....	1,024	1: 148	0.67
Totals Ablatio	281,608	1,170	1:241	0.42			
Totals Previa	327,448	.....	.....	....	1,657	1: 197	0.51

* If the incidence and the rate for ablatio were calculated upon the combined births of the "In and Out Services"—60,334—the incidence and the rate would be reduced to 0.57 per cent, i.e., 1:170, and 0.59 respectively. On the same basis the hypothetical incidence of previa would be 1:194, and the percentage would be 0.61. As the computations for the two hemorrhages are based upon hospital experiences they do not reflect the frequencies in the community as a whole; 1:500 for each would be a conservative conjecture.

No single procedure fulfills every purpose. One must weigh the evidence and employ the method which is indicated, and must elicit the conditions which will determine the appropriate course. The highly trained expert, in an ideal environment, may adopt methods which are not permissible for the attendant who may have occasion to treat a previa once or twice in a lifetime. The reader must scrutinize Table IV with a judicial mind, for the results obtained by the different therapies are not quite what they appear. For example, the circumspect will not select women for

Blood Transfusions. The replacement of lost blood when of material amount is imperatively required, for transfusions not only renew the blood volume but stabilize its quality, and greatly reduce the possibility of shock. They are so important that every institution which receives patients with puerperal hemorrhages should have facilities for their administration. The availability of donors and the possession of all the equipment for this purpose is no great problem in a large service, although in a small institution there are difficulties which must be met. These may be over-

come if a group of regional community hospitals coöperate to form a "blood bank" in the most centrally located hospital. Irrespective of the amount of blood loss, all hemorrhage patients admitted should routinely have a blood typing, blood count, and hemoglobin estimation. At the moment they may not be required but the timely investigation is more desirable than a hurried examination when an emergency arises. Where neither paid donors nor blood banks are available, a call should be made upon members of the family to come to the hospital for a grouping; then, the selected donor should stand by until it is clearly evident the blood will not be required. If blood is not available an opportune saline transfusion will raise the blood volume. According to the exigency of the case the saline should be given intravenously, subcutaneously, or rectally. If a cesarean section is performed, on indication, the instillation of a half to a full liter of decinormal solution into the abdominal cavity is invaluable, as suggested by Howard Kelly.

Of the various recourses in the treatment of previa, some are highly lauded, others condemned. The measures are: (1) temporizing; (2) awaiting spontaneous birth with such minimal ministrations as rupture of the membranes; (3) vaginal tamponade; (4) hystereurysis, either awaiting subsequent spontaneous labor, or more commonly, the internal version; (5) Hicks' version; (6) Willett's forceps, either as the sole expedient, or as an adjunct to other methods; (7) cesarean section; (8) accouchement forcé, including Dührssen's incisions and vaginal cesarean section; (9) management of the third stage.

TABLE VI

FREQUENCY RATES AND GROSS MATERNAL AND FETAL DEATH RATES IN ABLATIO PLACENTAE*

Authority	Total Deliveries	No. of Ablatios	Percentage	No. of Ablatios	No. of Maternal Deaths	Percentage	No. of Ablatios	No. of Fetal Deaths	Percentage
Goodell† (1870)	.....	.....	....	106	54	50.9	106	100	94.4
Holmes† (1901)	.....	.....	....	189	61	32.2	184	158	85.8
Willson‡ (1922)	.....	.....	....	69	31	44.9	67	62	92.5
Holmes (1922) personal cases	.....	.....	....	22	2	9.1	22	13	60.9
Cragin (1916)	20,000	212	1.06	212	12	5.7	212	122	57.5
Harrar (1917)	100,000	254	0.25	254	22	8.7	254	158	62.2
Burgess (1925)	18,720	80	0.43	80	6	7.5			
Fitzgibbon (1926)	55,000	115	0.20	115	11	9.5			
Brodhead (1927)	16,500	34	0.20	34	9	26.4	34	29	85.3
Kraul (1927)	15,000	27	0.18	27	2	7.4	27	17	62.9
Goethels (1928)	12,032	128	1.06	128	11	8.6	128	79	61.5
Wing (1928)	60,000	164	0.27						
Bartholomew (1929)	9,208	61	0.66	61	4	6.5	61	51	83.5
Williams	9,000	57	0.63	57	4	7.5	57	41	72.5
Davis-McGee (1931)	40,000	164	0.41	164	12	7.3	164	98	59.7
Irving (1937)	60,334	353	0.59	353	18	5.1	357	170	47.6
Bland-Rakoff	.....	.....	....	2,319	146	6.3	2,319	1,539	66.4
Totals	415,794	1,640	0.39	3,962	290	7.3	3,702	2,379	64.3

* After Davis and McGee, Irving, and the literature.

† The mortality data of Goodell and Holmes were not included in casting the total mortality rates, as the cases were treated from the early eighteenth century to 1900. They are given to contrast the old and modern mortality rates.

‡ Willson's sixty-nine cases were proved examples of Couvelair's uteroplacental apoplexy.

Temporizing. Placenta previa is a malignant affliction which demands prompt eradication. From the moment the physician becomes master of the field he should not retire until the patient is safely delivered or dead. Procrastination is disastrous. If an exception does exist it should be limited to the elderly primigravida, or childless parous woman, where a future pregnancy may no longer be a possibility. The physician should raise every objection to a delay, should positively explain to the patient and family the foolhardiness of such a course. It is a wise precaution to have his behests in writing, and a documentary evidence from them that the patient's imperious demands for the safety of the child outweighed any anxiety for herself. The patient must be hospitalized during the entire period of waiting and she must never be left alone. Written instructions should be in the possession of nurses and interns so that immediate action may be taken if bleeding recurs. A second hemorrhage should brook no delay.

Spontaneous Labor—Rupture of the Membranes. Singly or in combination, these methods are especially applicable to lateral and marginal previas and they may also be considered where a placental portion, torn away, is pendant in the birth canal. The prerequisite condition are: (1) the fetus must have a cephalic or breech presentation; under no circumstance should a shoulder present; (2) there must be no impediment to delivery; (3) hemorrhage must not be profuse. It is very desirable that there shall be uterine irritability, or, better, a definite onset of labor. The vulvar field should be surgically prepared for delivery, the membranes ruptured, and the liquor amnii be permitted to drain away slowly. It is well to keep the fingers in the vagina while the fluids are escaping so that one may determine that the fetal pole is descending. This process will permit the fetus to compress the bleeding surface. Watchfulness is imperative. If spontaneous delivery does not eventuate, then, when the presenting part is deeply in the pelvis, either a low forceps or modified manual aid should be carried out, as indicated. The extraction must be performed slowly, never hurriedly. This is the safest procedure for mother and baby as it obviates a major operation.

Tamponade. The use of the vaginal tampon is to be deprecated. It is rarely used by the specialist, but for the man of limited experience it is a very safe method. If the woman has had a dangerously severe hemorrhage, even a slight one, and must be transported to the hospital, it hardly seems justifiable to avoid its use. The memory of a physician who was called to a patient under allied circumstances is ever fresh. He felt it his duty to get the patient to the hospital promptly; the moment the woman was in the ambulance he rushed ahead to get the operating room prepared, but when the patient arrived at the admission door she was dead from hemorrhage.

The technique of applying the tampon is of extreme importance. The vulva must be thoroughly prepared. If the bleeding permits, the vagina may be swabbed out with mercurochrome or other approved antiseptic. Strips of gauze are inadequate. Sterile absorbent cotton must be used. The pledgets of cotton (the size of hickory nuts) are soaked in an approved antiseptic solution, as liquor cresolis or mercurochrome. The antiseptic is necessary so that putrefaction may be minimized. A large speculum is introduced and held in place by two fingers of the left hand in the vagina. The right hand passes the pledgets into the vagina, and the left fingers build up a firm ring about the cervix. Whenever a depression is found, a piece of cotton is crowded into it. The tampon must be tightly applied, as otherwise it is useless. When the packing has been completed, a large vulvar pad is applied and is held in place by means of a T binder. Under no circumstance should the tampon be left in place longer than twelve hours. The tampon is removed in the operating room, with a complete set-up provided. One may do one of three things when the tampon is removed,

depending on the condition of the cervical canal: (1) a hydrostatic bag may be placed; (2) a Hicks' version performed; or if these are impossible, (3) then one may repack until labor has progressed sufficiently to suggest that dilatation has occurred, when an internal version may be done. While repacking is strongly inadvisable it may be the best course if the attendant be inexperienced.

Hystereurysis. The bag is invaluable in a clinic where there is a frequent call for it, and where replacements are readily obtained. In small community hospitals where the bag may not be used over periods of many months, the rubber and the fabric may so deteriorate that bags are out of the question. Another objection is that once the bag is in place, the whole operating room force must remain for immediate action if the bag is expelled. If the cervix is soft and relaxed, the bag may be extruded in a very few minutes, while if it is firm and labor is not induced, many hours may elapse before it is forced out. The writer was once called to a small hospital where a bag had been employed for a previa. The operating room force went about their various pursuits, leaving the patient to a nurse to watch. The bag came away unexpectedly and before the staff could be reassembled the patient was exsanguinated, and she died shortly.

After the bag is in place and the stem ligated (never using an artery forceps for the purpose)—a 2 pound weight is attached to a cord extending to a few inches from the floor. It is a wise expedient to ligate the stem at the vulva that there may be a marker to denote the descent of the bag as dilatation progresses. If progress is not made within twelve, or at the longest, eighteen hours, the bag should be removed, and a fresh one inserted, unless sufficient dilatation is present to permit Hicks' version. In some instances the os is so closed that a version may not be done, so that a bag is employed to secure enough opening for the Hicks' maneuver.

The bag is invaluable in marginal, the so-called partial, and even for central types. It should invariably be inserted intra-ovularly. When placed within the sac it compresses both the placenta and its site, and has the advantage that since it rests on membrane which will eventually be expelled. If placed extra-ovularly it efficiently controls the placental site, but does not do so to the placenta, and may cause additional placental separation: the dangers of sepsis are more acute as the bag rests directly on the denuded site. In incomplete forms it merely is necessary to rupture the membranes before insertion. In complete cases, if an edge may not be palpated, the placenta is perforated and the bag passed through the rent. In every case the bag must be distended with a sterile fluid. If the bag is used as a preliminary measure before a Hicks' version, or if later an internal version is accomplished, the fetus invariably must be left for spontaneous expulsion —under no circumstance should there be rapid extraction.

Hicks' Version. During the near 60 years since Braxton Hicks devised the combined external and internal version which bears his name it has stood the test of time. It is conceded to be the best method, especially if the fetus is dead, for those whose training makes them an adept in the technique. There is no question but that the fetus may be turned with consummate ease if there is ample liquor amnii, yet many times the task is so difficult (as in oligohydramnios) that it tries the most expert. The bleeding which may accompany the procedure is disconcerting to an untrained man.

The os must be dilated sufficiently to admit two fingers, the vagina sufficiently relaxed to admit the hand, the membranes intact, or so recently ruptured that no retraction has taken place. The ideal is so to manipulate that the membranes are not ruptured until about the time the leg is to be brought down. The operation is contra-indicated in the presence of actual cervical rigidity, but the cervix unprepared for

dilatation may be relaxed by means of preliminary use of the rubber bag. A cervix unprepared for delivery is not to be considered one of rigidity. Cervical rigidity has been often certified to have warranted a cesarean section. However, personal communications from seven authorities (in 1905) with a total of 626 previas stated that the authors never had seen a true rigid cervix associated with previa.

The great advantage of Hicks' version lies in the fact that the smallest part of the fetus (the breech) passes through the cervix first, and the largest part, the head, last, so that the bleeding area is constantly being compressed.

Willett's Forceps. These forceps are a modified volsellum whose purpose is to permit traction on the head. They grasp the fetal scalp, and are applied whether the infant is alive or dead. It is alleged that they are harmless, but as the fetal mortality with their use is fairly high it is presumptive evidence that they do offer risks to the baby. The forceps must take a sufficient bite of the scalp or else they may pull off, thereby lacerating the tissues. It is claimed that they are applicable before a Hicks' version may be done, as only one finger dilatation is prerequisite, but as they must be applied blindly it is difficult to believe that they may always be effectively clamped to the head.

F. J. Browne found that this instrument was used 252 times, with a maternal mortality of 3.5 per cent and a fetal mortality of 46.4 per cent in a series of 3,103 previas treated in eleven teaching hospitals. He protests against their use, as asphyxia is produced since the head compresses not only the maternal placental circulation but that of the fetus as well. These allegations are spurious since this is the desirable effect in the use of the bag and the breech expulsion after any type of version. The compression of the bleeding surfaces by the fetal body is the ideal way of arresting hemorrhage.

When the forceps are applied a weight of not more than 2 pounds is applied in the same manner as for the hystereurynter. These forceps should not be considered a means of dragging the fetus through the canal, but merely for the purpose of keeping the fetal head in close juxtaposition to the bleeding surfaces. The advantage of having the largest part of the fetal body coming through last (in breech) is more than a theoretic one. The use of these forceps is worthy of further consideration and trial, as it obviates definite risks incident to version.

Cesarean Section. The first cesarean section deliberately done for placenta previa was probably performed by Sligh (1892). He resorted to tamponades for over a day, used hydrostatic dilators, ruptured the membranes, and what else(!!), and then turned to cesarean section as a last resort. Mother and baby died. Between that time and 1905 some twenty-eight additional operations were reported. Inspired by Lawson Tait who stated he had no experience with obstetrics, and Deaver who knew surgery but did not know obstetric surgery, cesarean section became the resort of surgeons and general practitioners long before obstetricians had a chance to clarify the atmosphere by designating the principles which should guide clinicians in the selection of cases suitable for the operation. Before their preachments prevailed, sections were performed without regard to the mismanagements which preceded the interventions. Yet, as late as 1935 (Children's Bureau, Publication #223) forty-one previal deaths preceded by sections had prior tamponades, and others gave suspicion that operative attempts had been made from below. Truesdale (1903) issued this dictum: "*Cesarean section should be done before anything else has been tried, or not at all.*" Obstetricians have repeatedly iterated this behest, but with little avail. Cesarean section for placenta previa is the strongest arm we possess, in appropriate cases, and about the worst if there have been antecedent attempts at vaginal delivery.

Definite conditions should obtain to justify the procedure:

1. There should be a freedom from potential or actual sepsis.

2. The section should be the primary operation (tampons or bags shall not have been used, or other manipulations tried). A diagnosis of previa cannot be made without a vaginal examination; this should be done with the most meticulous regard to asepsis.

3. The woman should be in good condition with minimal anemia, for anemia begets shock and a vulnerability to sepsis which are the great contributors to the death toll. A timely blood transfusion combats these evils. At best puerperal morbidity is approximately twice as frequent as after all other methods of delivery.

4. The fetus should be alive, in good condition and not be a teras (as proved by *x*-ray), and the pregnancy should have advanced beyond the period of prematurity.

5. The previa should be complete.

6. Abnormalities of the parturient canal offer strong contributory indications, such as contracted pelves or marked pathologic changes of the soft parts.

There is no question but that deviations from these strict admonishments may occasionally be demanded. When available, the expert obstetrician should be called to sum up the indications and the contraindications. At times, his acumen will be sorely taxed. Obstetric problems are inherent to the specialty. Good surgical principles do not always coincide with sound obstetric tenets.

It is advisable that a supravaginal hysterectomy follow the section if there is sepsis or if the patient has been exposed to vaginal manipulations. This operation was first suggested on theoretic grounds by Blundell (1834), but it is to the credit of Horatio R. Storer that he performed the first operation on a puerperal woman some ten years before Porro published his paper. This essential step must ever be kept in mind by those who manage a previa by cesarean section, as a precaution against a septic death. It may also be required if there is excessive uterine atony.

Whatever merits lower segment cesarean section may possess over the classic procedure for diverse indications, it still remains a moot question in placenta previa. In the years past many sites for the classic incision other than the anterior midline were elected to obviate the putative risks of a placenta previa cesarean. Some of the arguments against having the incision in the placental site were valid, others were rather illogical. We agree with Irving that there are definite objections to the low section for previa and that the management of the third stage may be controlled better through the classic cut. There may be, and often are, gross textural changes in the lower segment and cervix incident to the abnormal implantation. This, coupled with the risk of miscalculating the length of the incision in cervical cesarean section, may cause a deep tear into the portio vaginalis. The common necessity of readjusting the position of the head and application of forceps may cause additional placental separation and hemorrhage—and certainly delays the extraction of the fetus. In addition, the classic operation may be more quickly performed than the low section, and is better for the casual operator.

The average maternal mortality of cesarean section for placenta previa is 6 to 7 per cent, as given by various statisticians; in special clinics the rate is lower. The fetal death rate is 55 to 60 per cent, though Irving reports a gross fetal loss of 23 per cent.

Contracted pelves offer the great typical indication, if the mother and child are in perfect condition, where there may be a minimal loss of life. Anesthesia and some rare contingency may determine death. The operative risks are invariably present, but when the indications per se indicate high maternal and fetal dangers the operation carries a dual load. Cesarean section is neither a simple nor a perfectly safe operation. In 1929, 335 hospitals reported to the White House Conference 4,889 cesarean sections with 292 deaths, or 5.97 per cent. Of these, 161 hospitals reported 1,625

sections without a maternal death. Therefore, the remaining 174 institutions had 3,264 operations, among which were 292 deaths—8.9 per cent. Of these 174 hospitals, ninety-seven (55 per cent) with 776 operations had a death rate of 20.7 per cent. In fifty-three hospitals the rate was 32.2 per cent; in thirty-three it was 44.2 per cent; in eighteen it was 60.5 per cent; and in seven, with eight operations, it was 100 per cent. In 190 reporting hospitals the fetal death rate was 8.79 per cent; sixty-four hospitals with 413 operations lost no infants. The hospitals with reported deaths had a rate of 10.0 per cent; seventy-eight hospitals lost over 10 per cent of the infants; thirty-five lost over 20 per cent; twenty-two, over 30 per cent; eleven over 40 per cent, and in five, the ten babies died in ten operations.

How much the average death rate has been lowered these ten years may be proved by a comparable comprehensive study. Placenta previa is a fortuitous circumstance, not to recur. During the rest of the woman's reproductive life hovers the menace that if she conceives again and attempts a spontaneous labor a rupture of the uterine scar may occur with its calamitous result to her and her baby. At best, in each pregnancy she requires a terminal section to evade the accident.

The postoperative course, at the very best, is fraught with a potential morbidity. At least half of all patients with cesareans for placenta previa run some febrile reaction indicative of a degree of infection which jeopardizes the integrity of the scar. The writer has always taught that puerperal "morbidity" was a euphemism to gloss a low grade infection. The old axiom, "once a cesarean, always a cesarean" cannot be disregarded.

Conditions being as they are, we feel that cesarean section is not to be recommended as the happy means of treating placenta previa, though in some instances it is the only wise course. Promiscuity in its use cannot be condoned. One of the vaginal methods of management should be elected by the general practitioner. If the abdominal route is deemed the logical means of termination of the case he should select the best available abdominal surgeon to relieve him of the responsibility. *Make the section the primary operation—do not select the procedure as a wise solution after futile vaginal endeavors have accomplished nothing.*

Accouchement Forcé, Dührssen's Incisions, Vaginal Cesarean Section. These methods are grouped under one caption as objections to them are in a common category, and their effects on mother and child are unreasonably and dangerously high. The worst era in obstetric history was that period when brusque, even violent, measures were employed to accomplish a quick delivery. Manual dilatation, or the use of the Bossi type of instrumental dilatation, upon a friable cervix merely brought an unconscionably high mortality. Then to drag the fetus rapidly through a partly dilated or illy prepared tissue was but to complete what the artificial and rapid dehiscence failed to accomplish—a tearing high into the lower segment or into the parametrial structures. In those days, one-half the deaths resulted from the previal hemorrhage itself, one-quarter from bleeding from cervical lacerations, and the final quota from postpartum hemorrhage. Condemnation of this method is obvious.

Dührssen's incision and vaginal cesarean section are allied in that both must often be performed in a pool of blood which may interfere with the identification of the tissues and the determination of the extent of the incisions. They both necessitate immediate extraction of the fetus. Essen-Möller, after an experience with twenty-seven vaginal sections, severely condemned the procedure, and stated that one may never guage the proper length of the incision nor the extent of tearing which will ensue when the fetus is pulled through the opening.

THE THIRD STAGE

The dangers of previa are not over for the mother with the birth of the baby.

From the nature of a placental presentation, implanted upon the lower segment with its minimal retractility, aberrancies in the course of the third stage are frequent, though not necessarily constant. The more completely the placenta is located within the lower segment the greater is the likelihood of deviation from a normal course; per contra, the higher the lateral previa, the less the interference with the normal course of placental expulsion. Endometritis and deciduitis are not infrequently present and these are conducive to placental adherence. The lowered retractility and the general uterine atony induced by anemia are also factors. Further, the placenta is often lacerated to a high degree, and to the unwary may be the cause of a retention of placental remnants. Among them, these difficulties may produce a postpartum hemorrhage and cause the death of a woman already exsanguinated from ante- and intrapartal bleedings.

In the absence of bleeding, the following measures should be taken: The vulvar area is cleansed anew. A tape encircles the funis at the vulva to serve as a marker for the descent of the placenta. A large pad is placed over the vulva and the hand lightly controls the uterine fundus (noting contractility and retractility). The vulvar area is constantly kept under observation for undue bleeding, while the pulse and facies are frequently noted. When the placenta has left the uterus, as determined by the size, contour and the advancement of the cord, an Ahlfeld expression is practiced. At times the placenta will be spontaneously extruded. An ampule of pituitrin may be given immediately after the fetus has been born; this is especially indicated if there is any bleeding of consequence. Ergot and a second dose of pituitrin are indicated after the placental stage.

If there is any amount of bleeding in the third stage a Credé should be employed after message has secured a contraction, and not before. If bleeding is profuse, and massage and Credé fail to empty the uterus, a manual removal of the placenta should be carried out. Care must be taken that the placenta is removed intact; if tearing does occur there must be certainty that all placental fragments are removed. Every fragment should be kept, and an attempt made to rebuild the placenta into its original form so that one may be certain of total removal. If bleeding persists from atony or from lacerated cervical surfaces, a snug uterovaginal tamponade should be employed. Gauze, sterile and antiseptic, only should be used. The gauze should be in *one piece*, one-half yard wide, folded into a "tape" with the frayed edge folded inward, and 10 yards long. Depending on the size of the uterus (whether in prematurity or at term) 5 to 10 yards of gauze will be needed. The writer devised a uterine packer for this purpose some forty years ago and can vouch for its efficacy and safety. With its use the gauze touches no living tissue from its exit from the container until it is in situ.

SUMMARY

The essence of therapy for placenta previa includes these measures:

1. Arrest hemorrhage promptly (respect blood losses) by Hicks version, or by hystereurysis, or even by the objectionable tampon when needful.

2. Give timely *blood* or saline transfusions on indication.

3. Employ measures for delivery which are *slow* but sure.

4. Whatever the temptation may be, never practice rapid extraction of the fetus.

5. Circumspect management of the third stage.

6. On proper indication tampon the uterus and vagina—*never the vagina alone.*

7. Never repair the lacerated cervix unless the woman is in a remarkably fine condition. A secondary repair is always strongly desirable. If the tear bleeds the *uterovaginal tampon* will arrest it. A vaginal tampon is a transgression.

8. The routine swabbing of the vagina with an approved antiseptic (mercurochrome or liquor cresolis), where possible,

will sterilize the vagina to a degree: or these antiseptic may be instilled into the vagina by means of a catheter. Bichloride of mercury is absolutely contraindicated where there is blood or its serum, as was pointed out by Lister himself.

ABLATIO PLACENTAE

The separation of the normally situated placenta, or other designating terms credited to be synonymous, do not define specific entities, but are generic, covering a protean group which have two outstanding characteristics in common—placental separation and sequential hemorrhage. Our knowledge of the broad subject has sufficiently advanced to permit a segregation of the variants into four etiologic groups. The future will determine how much further this number may be extended as the specific causes are recognized. Then the symptom complex for each will probably be clearly appreciated, permitting a clinical diagnosis as the types present themselves. In fact, the toxemic forms may be so differentiated at the present time.

Since A. C. Baudelocque (1804) described and named a type of detachment where the entire blood loss was retained within the uterus, clinicians have recognized concealed and open hemorrhages. The difference is an interesting phenomenon, but every sign and symptom which occurs in the one is equally prominent in the other. Overt bleeding must never be taken as the diagnostic sign, but should be considered merely a corroboratory evidence. The diagnosis must be based on the facts, and should not await external bleeding. As the Mayos put it, liver disease should be diagnosed before jaundice appears, not after. Complete retention of the blood is merely the result of mechanical processes; in the course of moments or hours the mechanical obstructions break down and some blood escapes. When bleeding becomes patent the amount which escapes is never commensurate to the amount lost to the circulation (stored within the uterus). In order to clarify the nomenclature the writer has taught that the bleeding is *absolutely* or *relatively concealed*. Other writers differentiate between incomplete and complete placental separation.

FREQUENCY

Several postulates must be conceded before we may derive an intelligent computation of incidence. First, there must be a division into cases of pathologic interest and of clinical significance. The pathologic type is fairly common: routine examination of placentae reveals that the maternal surface contains one or many small, old clots, indicative of a pathologic alteration of the organ with capillary hemorrhages. These will be found in one placenta in 100, or one in 200 inspections. They must be not confused with flocculi or minute masses from Schultze's retroplacental clots. From the clinical viewpoint these hemorrhages must be segregated from the cases of clinical import. Harrar (1917) stated the matter tersely in discussing the incidence rates, "we only included those cases which were of sufficient moment to permit a diagnosis, or required treatment." On this basis he cited that all types of ablatio occurred once in 170 deliveries in the ward service, and once in 1,085 births in the outpatient department. The latter figure probably reflects the incidence in the community as a whole.

As has been stated, both placentae previa and ablatio placentae in a technical sense may occur any moment after the chorionic cotyledons begin to assume the characteristics of a rudimentary placenta. Retroplacental hemorrhages are almost constant accompaniments of placental separations in late abortions, including the period of immature development of the ovum, and are comparable to the retrodecidual hemorrhages of the very early abortion. Cognizance of this is never taken in any estimation of premature separations; the hemorrhages are reputed

to be peculiar to the early interruptions of pregnancy.

ETIOLOGY

The alleged etiologic influences for the production of a premature detachment vie with eclampsia in the multiplicity of theories.

Predisposing Causes. Parity has been considered without ample proof as a contributory factor, but it is of small moment. Of the writer's 200 cases the parity was given in 156 and 19.2 per cent were in primiparae. Brodhead reported 21 per cent, Davis and Colvin 36.6 per cent in this group.

Age is of negligible influence. The placenta is the one structure of the human body (ignoring that it is a part of a parasite) which is physiologically extruded when it has fulfilled its mission; the line of cleavage is definitely present in the decidual stage, and persists until the senile placenta is shed. Mesnard (1753) fully amplified this anatomic fact and Jacquemier (1887) substantiated it, explaining that the enormous ramification of fetal and maternal vessels, with a delicate barrier between, offers an inviting field for apoplexy and placental separation. When their structure is altered by inflammatory reactions or degenerative changes their integrity is doubly jeopardized, only requiring an abetting influence to precipitate a severance of the union.

Direct Causes. Knowledge of the etiology has sufficiently progressed to warrant the assumption that at least four groups of causes may be enumerated and it is not chimerical to believe the symptom complex for each will be segregated, and a clear clinical differentiation between them will be possible in the future:

1. Casualties and trauma.
2. Pathologies—inflammatory or degenerative changes of the serotina.
3. Toxemias—possibly not one but several forms.
4. The uteroplacental apoplexy of Couvelaire.

Casualties and Trauma. It was natural for writers of the past to have sought diligently for a traumatic origin, sincerely thinking that "accidental" connated this, and not recognizing the correct sense of its fortuity. One of the ablest writers recently perpetrated this error. Of the writer's 200 collected cases, sixty-seven (33 per cent) were considered due to this cause, though over a hundred years ago J. Ramsbotham pointed out that there was not an immediate correlation of cause and effect. Some of the present authorities would decry the importance of injuries; of all the viscera of the body the growing uterus is the only one which is unprotected and directly exposed to attacks. We cannot escape the effect of trauma, though our modern conception of cellular pathology relegates it to a lesser rôle. When trauma does occur it is tragic in effect.

Bartholomew and Colvin aver that fetal movements, and J. W. Williams that hypertension, will cause separations when directed to degenerated villi; severe blows, jars, falls, whether directly or by contrecoup, may likewise be effective. We have an analogy in rupture of the abdominal and thoracic viscera, though no one has maintained that this can occur only in a diseased organ. Intra-uterine manipulations, such as version or the induction of labor by catheters, have caused the disaster of an ablatio. Gendrin (quoted by Cazeaux and Tarnier) maintained that contractions alone were causative, and the contractions and retractions following the birth of the first of twins, or the precipitous evacuation of a polyhydramnic fluid have sometimes been responsible. The short cord may pull the placenta from its attachment; in the writer's collection six instances were recorded. We cannot deny that an outburst of emotions plays an important part. In the course of great public catastrophies many women will have severe hemorrhages and interruptions of pregnancy from this cause.

Pathogenic: Local Inflammations and Degenerations. An antecedent endometritis with a continuation during pregnancy

as a deciduitis has long been considered of importance in the production of premature separation. In such involvements it would be inevitable that the basalis would be affected. In the writer's series of cases reported before 1900, endometritis, deciduitis, scirrhus of the uterus, exudative myometritis, and "fatty degeneration of the decidua were mentioned."

Rokitansky described placentae which had inflammatory deposits in the lobules expressed in a thickening of the endothelium of the terminal circulatory vessels, even obliterations of the capillaries by thrombosis. Infarcts were often mentioned. Slow infarction is the characteristic of a large proportion of all senile placentae. As far back as Fehling (1887) infarctions played an important part in the discussions on the cause of ablatio. He and Schroeder (Ohlshausen and Veit-1899) asserted that we must go further before we may declare infarctions in women with nephritis different from those in normal placentae. This matter on which Bartholomew and Colvin have made many enlightening pronouncements, will be resumed in its appropriate place.

Fatty degeneration, present in senile afterbirths, has been stressed as a causative factor. Fibrosis of the placenta has been a putative element. Calcareous degeneration in the nonpregnant uterus is known to be accompanied by hemorrhages. Calcareous deposits in the placenta may hold an allied position. Though calcification is present in presumably normal placentae, it is logical to believe that this factor may be causative in the presence of a strong impulse, as is the case in cerebral apoplexy.

However, many placentae in traumatic or spontaneous ablatio show no morphologic changes other than the markings of a senile organ.

Syphilis has long been known to produce gross and microscopic alterations of the placental structure. Spirochetes have been isolated in the organ, yet this disease holds but a minor place in the etiology in spite of its widespread prevalence. Syphilis as a coincident or direct etiologic factor was recorded in four cases in sixty-four reports where cause was cited—6.3 per cent. In only two of the 164 cases reported by Davis and McGee was there a positive response to Wassermann and Kahn tests—1.2 per cent.

Hofbauer experimentally produced a state allied to ablatio by the injection of histamine into pregnant animals, though at the Chicago Lying-in Hospital his findings could not be corroborated.

Toxemic Types. These must be presented collectively as it is not known whether the varying intensities are due to differences in the amount or virulence of a specific poison, or to a number of diverse intoxicating substances. A profound stimulus was given to general nosology, and to obstetrics in particular, when Brown-Séquard and his disciples promulgated the new theory that diseases could be engendered by noxious substances elaborated within the body. Toxemia, however, was not a new term, for obstetricians used it nearly a hundred years ago to designate a poisoning, not from ingested substances: the word was as comprehensively applied as the obsolete "miasm."

A second great contribution came with the development of the knowledge of endocrinology. As fantastic beliefs were sifted out by earnest investigators, hypotheses were evolved that toxemia was the result of aberrant metabolism, and to this, later, was added the influence of normal or abnormal internal secretions. We know the profound influence of thyroid and pituitary extracts upon ovarian function and upon the whole ovarian and uterine cycle. Malign mutations might be carried into the whole reproductive process. The ovum, and later the fetus and placenta, may have their own endocrine and metabolic by-products which may have a warring effect on the maternal host and her biochemical reactions. The nebulous theory of the protein reaction of the fetus upon the mother is indicative of this. It must be true that the fetus and the placenta may acquire disease and degeneration independ-

ent of the mother which will be adverse to the maternal welfare, as the reverse is indubitably true.

Time only will show the value of our theories. New hypotheses will be developed and discarded. Old notions will be revived as their tenableness is verified. Who would believe that the denial of Fehling (1887) that infarcts were germaine to ablatio would redound to his discredit, and that it remained for Bartholomew and Colvin to show that certain forms of infarctions were definitely correlated to toxemia, with special association to toxic placental detachments? This is a real progress even though the exact correlation between them has not been conclusively defined.

A new impetus was given to the study of the causes of placental detachments when Hennig (1875) demonstrated the presumed connection between them and albuminuria. Winter (1884) and Weiss (1894) substantiated Hennig's postulate by reporting cases where the two were coexistent. Lehmann (1899), cited the report of Rousseau-Dumarcet showing albuminuria in eleven of twelve instances of detachment, and in twenty-four of thirty-one examples of detachment in the Clinique Baudelocque. It was epochal when Desmond (1857) and Weiss (1894) recognized the ecchymotic spots on the uterus, though it became the honor of Couvelaire (1911) to interpret them correctly.

It has been alleged that chronic nephritis gave a woman a relative immunity against a possible placental separation. Williams, Frankl and Heiss, and Davis and McGee respectively stated the incidence rates to be 3.5, 3.9, and 9.6 per cent. The New York Lying-in Hospital in 1934 reported a frequency of 1.38, and in 1937 0.82 per cent for chronic nephritis. The assumed security of chronic nephritics against a placental detachment is not verified by facts. *Eclampsia* has been declared akin and even identical with toxic placental separations. It was assumed that under different circumstances the poison had a peculiar selective action, on the liver in the one, and on the uterus in the other. In the combined collection of Goodell (106 cases) and of the writer (200 cases), J. T. Ingleby, J. L. Baudelocque, Hennig and Tucker reported the coexistence of detachment and eclampsia. The writer presented two instances of eclampsia-ablatio in his twenty-two personal cases. The combination occurred 6 times in 328 cases, or 1.8 per cent. In the sixty-seven cases of Couvelaire uteri collected by P. Willson (1922) the double disease was noted in six, 8.6 per cent. Harrar found the duality in 1 per cent, Davis and McGee in 0.61 per cent. In 1922 the writer stated, "It is plausible to believe that the concomitant presence of eclampsia and toxic ablatios is a manifestation of the activity of two foreign substances arousing diverse syndromes."

PATHOLOGY

The pathology may vary macroscopically and microscopically from normal or insignificantly changed placental values to slight mutations of the placenta and uterus, or to such extreme changes that even distant viscera are markedly altered. A retroplacental clot is almost invariably found, irrespective of the etiology. The absence of old black clots, expelled with the placenta, strongly indicates that an error of diagnosis has been made. If the egress of blood is mechanically prevented, free sanguinous fluid bathes the clot, and commonly is discharged with the placenta, at least in part. The clot is either free in the uteroplacental cavity, sessile and adherent to the maternal surface, or, if the periphery of the cavity has remained adherent for a sufficient time, the coagulum will fill a depression on the maternal surface of the placenta. While the clot is distinctly fresh it is soft, compressible and of normal reddish appearance. As time elapses it blackens, contracts, extrudes its serum, and becomes firm. The independent studies of Rokitansky and Spiegelberg and Brodhead have demonstrated that not infrequently similar but smaller clots will be found in mature placentae as the result of unmani-

fested slight hemorrhages long antedating the labor. Spiegelberg found them present in fifty-seven of 5,900 inspections, Brodhead in seven of 1,000 placentae examined at term. One or many such clots may be distributed over the maternal surface, varying in size from a millet seed to considerable dimensions. In one case a woman was severely hit over the uterus, collapsed, was revived and went to term. Here the clot was the size of a goose egg. These clots, having endured for a protracted period, are very firm, the color of dirty putty, due to the absorption and disintegration of the hemoglobin. Separations and hemorrhages, it is believed, result from isolated degenerative changes in limited areas.

In cases of trauma, or inflammatory or degenerative processes, comparatively little illuminating change is present. At times the appearances of the uterus and placenta are those normally present. However, gross cellular morbidity may be revealed. The infarctions may be more pronounced than normal. They may vary in color from old white to comparatively new areas in which the hemic elements are still in early decomposition. The reddish to white infarctions may be large and cover a considerable portion of the maternal surface, or may even be buried within the placental tissue. Placentitis may be recognized by a profusion of capillaries undergoing thickening and thrombotic obliteration. The serotina is likewise thickened. There may be connective tissue proliferation, showing a variability in the development of sclerosis.

Toxic Pathology. The diverse pathologic changes in the tissues of women seized with toxic ablatio leads to the conclusion that there are at least two distinctive noxious substances which produce different types of toxemia, one the ordinary form, the other the Couvelaire type. It is hardly tenable to hold that diverse effects are the consequence of a single element varying in virulence, even though we have not clearly differentiated the two clinical types.

In ordinary toxic ablatio, the kidneys are generally involved in varying degrees. Albuminuria, casts, and some hematocyturia are expressive of an acute nephritis. Microscopic specimens show involvement of the cortical layer and the glomeruli. The liver rarely reveals special alterations beyond a possible cloudy swelling. The gross appearance of the liver is unaltered. Microscopic study of the placenta may show normality or hypertrophy of the vascular intima, with, perhaps, a connective tissue proliferation. These are particularly evident adjacent to the placental site. The placenta contains a number of infarcts of recent origin, brown or brownish in color. The white ancient infarcts are present in nearly all normal placentae, but in ablatio may be larger. They may be on the maternal surface or buried within the structure. In a few instances the escaping blood has a port wine hue, and is watery with little or belated coagulability.

Uteroplacental Apoplexy. The poison produces extreme permeability of the vascular supply of the affected organs, with widespread hemorrhages, thromboses, or extensive penetration of free blood in the tissues. Extremely rapid coagulation results after the blood has escaped the vascular intima. Extreme hemolysis may occur at one point, and retention of normal characteristics at another. Cellular lysis, wherever the blood bathes the tissue, and marked leucocytosis occur with great predominance of the polymorphonuclears. There is a dearth of literature on blood analyses of toxic patients in whom premature detachment is likely or has actually occurred. Hemal studies prior to the explosion and afterward could elucidate many moot problems. Ultimate knowledge of etiology will be as certainly discovered from clinical investigations of the blood as from shed specimens or from tissues obtained post-mortem.

In 1923 the writer reported a case of toxic apoplexy, in which the placenta and uterus had a wide distribution of polymorphonuclear leucocytes, not only in the fetal and maternal blood streams, but also in the extravasated blood. Unfortunately

blood counts had not been made before operation. Since then we have taught that the blood examination should be a routine part of the antepartum investigation. Serial study of numbers of cases would tend to prove whether polymorphonuclear leucocytosis is a peculiarity of toxic apoplexy alone, or present in all ablatios. If it is limited to the toxic apoplexy, a valuable diagnostic aid would be available. If it is present in all premature detachments it would resemble the state obtaining in ruptured ectopic where the white count may rise to 15,000 or even 40,000.

The kidneys are almost invariably involved. There is a high grade cortical degeneration, thrombi are often found, and the glomeruli and the tubules are markedly impaired. The thrombotic process may be so extensive that in a few instances the cortices of both kidneys have been entirely disintegrated. The liver may present corroborative evidences and subperitoneal hemorrhages, from petechia to those of material size, may be present. These retroperitoneal hemorrhages may appear elsewhere in the abdomen, but they are always superficial extravasations. In the loose areolar tissue of the broad ligaments or beneath, hematomatous formations are sometimes noted, though they are exceptional. Within the liver there are hemorrhagic infiltrations distant from the portal areas. Necrosis is not invariable. These hemorrhagic spots are clearly distinguished from those seen in eclamptic liver degenerations.

The gross appearance of the uterus is extremely characteristic: the subperitoneal surface is blue-black to purplish in color; the ecchymotic splotches may cover large areas of the organ, or they may be small and multiple; they rarely are regular in outline, but rather are peculiarly rimmed with digitations. The variations in extent probably reflect the intensity of the venom. The adnexa may or may not be involved. In some instances the peritoneal surface is striated from superficial rupture of the serous coat. Serous fluid or free blood is rarely found in the abdominal cavity. The cut surfaces of the uterus reveal wide diffusion of the extravasated blood, particularly in proximity to the placental site, and under the peritoneum and mucosa. Microscopic examination reveals the extensive diffusion of blood. In one place large muscle bundles are separated by massive extravasations, while in others, the fasciculi are bathed in blood or individual fibers dissected from one another by the blood. The intima of the vessels is thickened, the vessels may be filled with liquid blood or there may be thrombi. Wherever they may be differentiated, as in the writer's case, the polymorphonuclear leucocytes are greatly increased, even proportionate in number to the erythrocytes. The connective tissue may show some feeble attempts at proliferation, and the cells of the muscle tissue exhibit the effect of a cytolytic action.

The placenta may be extremely involved. Fresh infarcts, black to brown, may compromise extensive areas, so that in some cases considerable portions of the placenta are affected. The infarcts are more fragile than the contiguous normal tissue. On microscopic examination the same blood extravasations are apparent. The larger vessels may be distended with free blood, which later is coagulated. The capillaries have the same relative appearance, with, now and then, ruptured walls. The cellular tissue is thickened and undergoing degeneration. The rupture of the vessels, if the serotina is torn, may contribute the thought that the primary retroplacental blood is maternal with some admixture from the fetus.

MECHANICS OF PLACENTAL SEPARATION

The repercussion resulting from an injury may well be the cause of a loss of continuity of the uteroplacental union, the cavity thereupon becoming filled with blood. This hardly can be the case where the causal factor is of the pathologic or toxic types. Under these circumstances the apoplexy in the serotina is primary, the escaping blood forming its own antrum, unless we may conjecture that the diseased

area has so degenerated that there is a primary disjunction. If the disrupted area is central and the surrounding serotina normally adherent, the physiologic adhesion effectually dams the effused blood. The blood becomes a foreign body and stimulates uterine contractions. Contractions tend to diminish the capacity of the cavity, but acting upon the incompressible blood and clot, will force the latter to burrow its way afield. During each interval of relaxation additional blood will enter the cavity. Progressively, in this wise, supplemental separations occur until eventually the open space reaches the periphery.

All this time the bleeding is entirely occult and thereafter other factors may maintain the concealed hemorrhage. The first of these is a firm adhesion of a dense chorion, possibly the sequel of an endometritis. The second factor is that the membranes may rupture adjacent to the placenta, and the blood mingle with the liquor amnii. This putative cause of retention is hypothetical, as the opening has not been observed. However, when the membranes rupture at the os, free blood and clots are coincidentally expelled. Again, the presenting part—head or breech—may be so firmly depressed within the cervical ring that it serves as an effectual barrier. This is a constant factor, as frequently blood is discharged with the expulsion of the fetus and placenta—conclusive corroboration of antenatal separation. Again, a few examples of conglutinatio orificii externi have been reported which prevented any overt hemorrhage. Finally, in some examples of the Couvelaire apoplexy the blood coagulation is so prompt that there is no free blood to escape. Such are the dynamics of total concealment of the hemorrhage, which must be interpreted as the first cycle of uterine hemorrhage incident to antepartum separations.

The second phase of the hemorrhage is when blood escapes from the vagina. This may occur immediately in relation to the appearance of the primary symptoms, or may be delayed for many hours. The first sign of external bleeding may be manifested in one of two ways, dependent upon the interval between the onset and the time when a canalization has developed between the detached placenta and the internal os. If the interim is short the bleeding may appear as a seepage, or it may be of material amount expressed by free blood or clots. If the interval indicates considerable chronicity, the restrained blood coagulates, the clots contract, extruding the serum which finds its way to the os, appearing as a pinkish fluid which may be scanty or profuse. In one case of the writer's, it was so abundant that it saturated the underwear and dress, so that the attendant deemed it to be liquor amnii: such serous discharge was noted in five (23 per cent) of his personal cases; in the compilation it was recorded in twenty-two (11 per cent). Careful observation will determine this evidence of internal bleeding far more frequently than is generally supposed. In due course free blood will follow the serous discharge.

Finally, the onset may be so precipitous that a massive separation and a hemorrhagic deluge may take place before succor can be of any avail.

Two anomalous forms of premature detachment are worthy of mention; that of separation, prolapse, and extrusion of the placenta before the fetus, and complete thrombosis of the sinuses with separation but without hemorrhage. Feinberg, Hüter, Anderson and Haberlin reported such examples and Feinberg and Münchmeyer each cited a case of the latter.

SYMPTOMATOLOGY

Some authorities have described an array of symptoms which are supposed to be characteristic of a typical ablatio. It would be caviling to question the evidence that in some instances pronounced signs and symptoms are unequivocal, but these are classical examples from which must be evolved the symptom complexities which accompany aberrant courses. One case may

be recognized instantly, while in others hours may elapse before a true conception is reached. The most bewildering implications may appear during the early hours, and then some final special signs will develop which permit a conclusive diagnosis.

The symptoms of retroplacental hemorrhages are protean in their manifestations, varying under diverse conditions and circumstances. The mutability of the criteria of ablatio offers a striking contrast to the signs of placenta previa. Both follow placental separation, both have hemorrhages, yet the hemorrhages of ablatio produce an array of startling reactions while those of previa produce but one—anemia. A minimal separation with blood restrained within a ring of firm adhesion will pass unnoticed, or, at most, will produce only vague transitory discomfort, while pregnancy continues unaffected. This may not be considered a clinical type.

A practical elucidation delimits three groups: (1) the mild; (2) the severe; (3) the fulminant. Each of these may be subdivided into absolutely and relatively concealed hemorrhages and again into partial separations and complete disjunctions of the placenta, and finally into etiologic types, as traumatic, nontoxic, toxic, and the Couvelaire uteroplacental apoplexy. Each primary group, from mild to fulminating has increasingly obvious signs and symptoms, though certain dominating characteristics may be in abeyance in individual cases.

All the manifestations of ablatio emanate from the retroplacental hemorrhage, producing local reactions or systemic effects. As the amount of bleeding is always masked, both before and after external showing, the amount lost may be judged in relation to the circulatory effects and by the general facies. The depictions are for the average woman; deviations in weight, physical condition (the large healthy woman may stand more, the weak, sickly, anemic one less). The cardiovascular system reacts more quickly to a slow bleeding, and more readily fails with severe gushes.

One Pint Loss. The prolabia and the conjunctivae are pale. The cutaneous surfaces show little or no pallor, and are warm. The pulse volume is of good quality, though the rate may be accelerated 10 or 20 beats; blood pressure readings may show some depression, respirations are unaffected or slightly faster. If erect, the patient may feel dizzy, but this is absent if she is lying down.

Two Pint Loss. The prolabia and the conjunctivae definitely lose all color, the skin is whitened and cool to the touch, especially in the extremities. Drops of perspiration appear about the lips, below the palpebra, and upon the forehead, and the skin generally is damp. The patient complains of faintness and may have repeated syncope. Nervousness is evident, even some restlessness. The pulse rate is materially increased—140–160, and its quality is soft and compressible. The blood pressure is distinctly lowered, both diastolic and systolic being 10 to 20 or more points below earlier readings. Respirations are clearly accelerated, and the patient complains of aches throughout her body, repeatedly mentions her weariness and experiences intense thirst.

Loss of over Three Pints. The exposed mucosa is colorless, the skin cold, clammy and alabaster or even waxy, much of its elasticity lost. Beads of perspiration appear about the head. The pulse is thready and extremely rapid, over 200; the diastolic pressure is extremely low, with feeble rises of the systolic; respirations are increased greatly, to 40 or more per minute, and are irregular with the accessory respiratory muscles labored. Facial grimaces and contortions as air hunger supervenes are distressing to the bystanders. Thirst is imperious. The woman is extremely nervous, restless to a high degree, clamoring in her delirium, jactations will be pronounced. Throughout the ordeal she complains of the pains throughout her body.

The signs and symptoms are here discussed in the order of their importance rather than in the chronologic order; in

fact, the latter would be impossible as many of the diagnostic features appear synchronously.

Systemic Reactions. Faintness, Dizziness, Syncope. Their presence is dependent entirely upon the amount and the suddenness of the blood loss and the response of the sensorium. The manifestations may be temporary or persistent, but their significance is greater than their apparent intrinsic worth. The laity holds a high opinion of the lack of stability of the average pregnant woman, and tends to believe that such cerebral imbalance is a phenomenon peculiar to her condition. From the frequent belated diagnoses one must infer that some physicians also disregard this sign, which may be ominous. Every physician should determine promptly the basic cause for the cerebral anemia before he commits himself to its innocence; syncope may be the only symptom of rupture of the serotina obtainable until the patient regains consciousness. Before this time the physician must investigate the uterus.

Nausea and Emesis. These are other symptoms which are popularly regarded as normal characteristics of the pregnant woman. When they are associated with dizziness and syncope they warrant an especial endeavor to differentiate them from the supposed normal and from abdominal disturbances. The combination demands an examination of the uterus, as otherwise the opportunity for making an early diagnosis of detachment will be lost. In one case these signs were the only tangible evidences, and nearly ten hours elapsed before conclusive symptoms were sufficiently developed to permit a diagnosis.

Direct Evidences of Hemorrhage. The facies of the patient strongly indicates the possibility of hemorrhage (vide supra). The pulse rate, and a soft, compressible pulse also offer some suggestion. The enumeration of the erythrocytes and leucocytes, and the estimation of the hemoglobin content are vitally important. These data will be in the normal range if the first tests are made promptly after the onset, but are indispensable gauges for comparison with later serial examinations, hour by hour. The primary effect of hemorrhage is to reduce blood volume *only;* progressively, as the bodily sera are taken into the blood stream the proportionate cellular elements diminish directly as dilution increases.

Blood Pressure. The taking of blood pressure is an essential part of sane prenatal and intranatal maternal care. The lamentable thing is that too often this essential diagnostic detail is absent from reports. A mitigating circumstance is that a large majority of ablatios are admitted to the hospital in full flower. Yet, little or no mention is given to the interpretations of blood pressure. In two classic contributions on the several types of ablatio published within recent years, no comment is made concerning the use of the sphygmomanometer in one, and the other disposes of the matter in three lines. The writer (1923) stated: "It would be eminently desirable to have more recording of blood pressure readings in relation not only to the toxic types of placental separation, but in ordinary ablatios as well, for they may furnish valuable clinical data for the differentiation between them."

The sphygmomanometer is an essential appliance in all obstetric work. It is as invaluable when conscientiously used in the presence of possible or actual hemorrhage as it is in toxemias. In ablatio it serves a dual purpose: its routine use during the course of hemorrhage demonstrates the effect of the blood loss upon the circulation and in all types of ablatio where the blood is blindly stored up within the uterus it offers a better criterion of blood volume and content than any other measure. A falling blood pressure is an infallible index of continued bleeding and is the quickest means of determining the response of the body economy to proper stimulation.

Secondly, at least half of all ablatios are in some measure toxic, and blood pressure *may* give some conclusive evidence of the degree of the toxicity. This is true, even

though the next sentences are paradoxical. We are still in the dark as to whether the toxemias of ablatio are necessarily accompanied by a hypertension. True, most clinicians make the basic diagnosis of toxemia on the high pressure (over 140, systolic) and the urinalyses. The large majority of toxemic ablatios are first seen when the patients are institutionalized, and they will quite generally have hypertension. In contrast to this, some toxic types, as well as the virulent Couvelaire apoplexies, will have a normal rate or have hypotension. Couvelaire states that toxic apoplexy is not necessarily correlated to vascular lesions or hypertension. It is still a moot question whether this is due to absence of increased tension or to the depressive action of the loss of blood volume. P. Willson (1922) collected sixty-seven examples of the Couvelaire type from the literature: of these only nine reports had records of pressure readings; two were normal (100 and 120), and six had a range from 160 to 260 (160, 170, 174, 180, 200, 260), the patient with 280 having a coincident eclampsia. The writer's case of Couvelaire uterus, proved by cesarean section, had a pressure of 120.

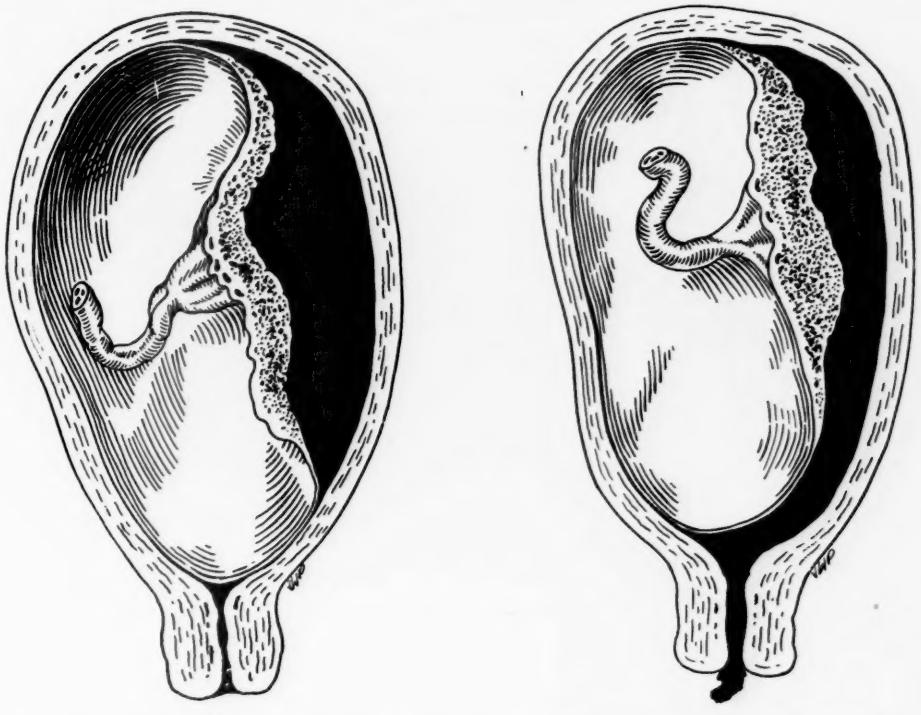
To restate the facts—the routine and conscientious use of the sphygmomanometer will supply us with fundamental knowledge of the connection between hypertension and all types of ablatio, both nontoxic and toxic.

The Uterus. All the rest of the signs and symptoms of ablatio emanate from the actions and reactions of the uterus and its contents. The whole behavior of these structures depends upon the response to the stimuli created by the intra-uterine bleeding. The restrained blood promptly becomes a foreign body. A small area of the placenta having separated with a minimal bleeding, there may be minor discomforts to the patient, but abnormality in connection with the uterus may be ignored. A major separation with a material gush of blood will usher in a train of violent reactions; the woman may be conscious of the distention going on and it has been reported that the by-standers have seen the uterus increase in size. The pain may range from the sensation of a distention to such a degree that the woman will clamor about it. In some few instances the concussion of a large, or total, separation may produce a rending pain which is comparable to that of the rupture of the uterus or of an ectopic pregnancy. A placenta which is located lower on the uterine wall, with its lower border separated may produce no distress whatsoever—it may readily be mistaken for a lateral placenta previa. On the other hand, a central separation or detachment of the upper border may be accompanied by a massive outpouring, violent pain, and classic findings. In the report of Davis and McGee *no pain* or contractions were noted in 8 per cent of the 164 cases. Pain is proportionate to the degree of separation, reaching its maximum with total separation. The uteroplacental apoplexy, where total separations are the rule, almost invariably produces pain.

Examination of the uterus divulges many important facts. *Tenderness* of the uterus, especially in the region of the placental site, is often found, though according to Davis and McGee, it is elicited in only 30 per cent. Where the uterus is distended with the major portion of the placenta separated tenderness is particularly noted. It is important to note the *consistency* of the uterine wall. In the author's 200 cases facts pertinent to this point were given in forty reports (twenty-two as tense, eighteen as boggy). The authors above cited state that tenseness (ligneous hardness) occurred in 29.2 per cent. It is still a moot point whether we should or should not reserve extreme hardness for the Couvelaire type.

The *contour* of the uterus should be observed by inspection and palpation. If there is wide diffusion of the blood it may be ascertained that the uterus is symmetrically enlarged with the normal ovoid. If the placental site is anteriorly placed (which occurs in about half of all pregnancies), and the blood is confined in a

circumscribed mass, there may be a marked irregularity, even a definite protuberance—always sessile—the *accessory tumor* of the



A B

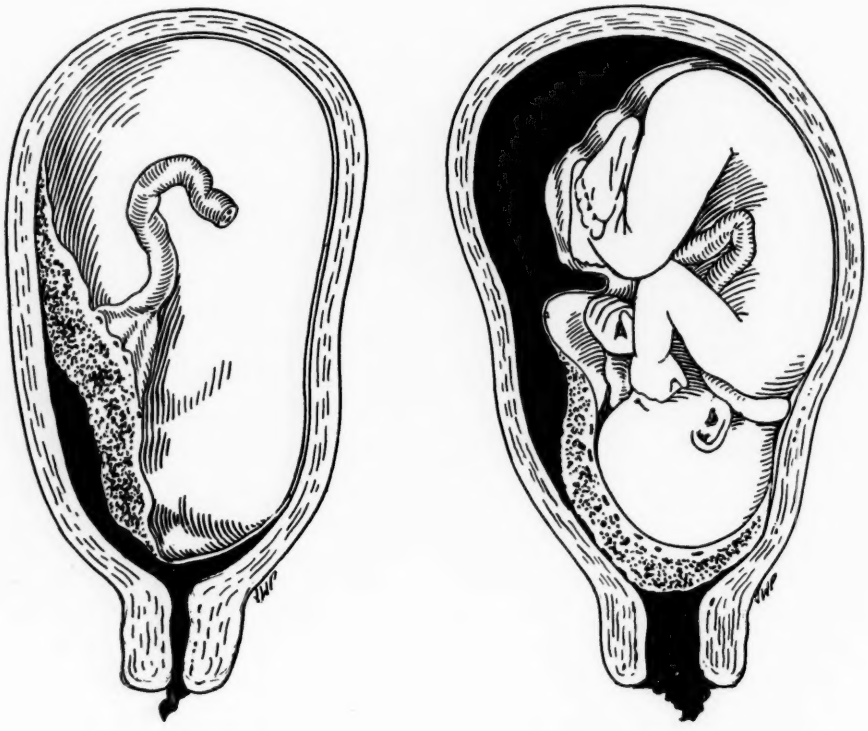
Fig. 1. Ablatio placentae. A, internal or concealed hemorrhage. B, combined internal and external hemorrhage. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

old writers. This is a characteristic finding, but must not be confused with a subserous fibroid. The tumor was recognized in fourteen cases of the writer's assembly—7 per cent; in his personally observed cases (twenty-two) it was noted in five (22.7 per cent). This sign possibly might be observed with twice the frequency if the posterior wall were palpable. If the placenta and clot are in a cornu, with the fetal pole in the other horn, a bicornuate uterus may be simulated.

The Fetus. After separation has occurred, a malposition is found in about 10 per cent of women, the fetus being crowded from its axial relations by the clot and dislodged placenta. A minor placental dislodgment allows the fetal heart rate and quality to be normal, but in material separation the heart tones indicate the fetal jeopardy by their gross irregularity and quality. Slow death ensues. If the separation is massive or complete, the patient often perceives violent fetal movements for a moment, followed by the quiescence of death. If the physician sees the patient early, the manner of eventual cessation of fetal heart tones may give some slight notion as to the degree of placental separation. The fetus in any case dies from asphyxiation, from the toxemia if present, and possibly from hemorrhage if the placenta is torn.

The Hemorrhages. Certain statements may be accepted as axiomatic. The total concealment of the blood is an inherent primary attribute of the diseases characterized by placental separations, irrespective of the generic name designated by the fancy of the user. The condition may result from trauma, pathology, of peculiarly local form, or from systemic dyscrasia as toxemia or uteroplacental apoplexy. The concealment is due to definite physical barriers which may be present in all intra-uterine hemorrhages, irrespective of cause, not alone in ablatio, but in certain uterine ruptures and in a few disintegrating submucous fibroids. If there are no barriers,

the hemorrhage of an ablatio may become external promptly, while if barriers exist, the concealment persists until uterine contractions or other mechanical processes raise intra-uterine pressure, thus destroying the barricade.



A B

Fig. 2. Ablatio placentae. A, external hemorrhage. B, external hemorrhage and prolapsus placentae. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

The external bleeding is merely a tardy corroboratory sign of the intra-uterine events comparable to the appearance of jaundice in liver disease or late hemorrhages in typhoid. It should be emphasized that there is not one sign or symptom present in totally concealed cases which does not appear in the patent types—except that the latter gives ocular evidence of blood. *The external hemorrhage under no circumstance is the gauge of the amount of blood stored within the uterus.* As a corollary to this we have an invariable diagnostic point, which substantiates all ante- and postpartal diagnostic features; with the child and placenta are expelled *all* the free blood and clots which were pent up in the uterus. The extruded blood is in inverse proportion to the blood discharged prior to delivery. We cannot subscribe to a classification which would include "all cases where the bulk of the hemorrhage was retained within the uterus are internal hemorrhages." We do not have positive criteria upon which to base the estimate of the amount of retained blood.

From the time of Goodell it has been believed that totally concealed hemorrhages carry a heavier toll than the open. The high mortality rate of "concealed" cases is not due so much to the fact of complete retention, as it is to the hours of needless waiting until a correct diagnosis is made. On theoretic grounds the complete retention of blood is nature's endeavor to conserve life, for the blood is dammed up. This is favorable if there is tonicity of the uterine muscle. The success, and it was an actual triumph in its era, of the Dublin method of treating accidental hemorrhage by vaginal tamponade relied upon this—converting a patent hemorrhage into an

occult one. The writer suggested the division into relatively and absolutely concealed hemorrhages, but such clinical forms

Fig. 3. Premature separation of the placenta with concealed hemorrhage. The uterus was removed by supravaginal hysterectomy, owing to the marked involvement of the uterine muscle. Williams' specimen. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

are not basic enough to permit their use for the computations of mortality rates. Too many factors, some clearly featured, and others too obscure for interpretation determine the death rates. The amount of blood lost, within the range of practical reason, does not always determine the cause of death. On the average the hemorrhages in traumatic and pathologic ablatios are excessive, yet we know the mortality rates for them is low. We know that the usual hemorrhage in Couvelaire's uterus is remarkably and relatively small, yet the mortality rate is high, because a malignant toxic substance saturates all tissues.

DIAGNOSIS

The introductory sentence in the discussion of ablatio expresses the conviction of the writer that we are not dealing with a specific disorder, but rather with a number of morbid states which are expressed by two fundamental crises—placental separation and concomitant hemorrhage. Subsequent actions and reactions are dependent upon the degree of placental separation, the location of the placental site, the amount of blood loss. The etiologic factor probably alters these influences as much, if not more, than the nervous and physical stability of the patient. There is such diversity in response to the separation per se and in the hemorrhage, that future clinicians will perhaps be able to unravel

the doubt by means of these differences. As it now is, generic ablatio has a kaleidoscopic presentation which is truly perplexing, varying in the same patient and in different patients. It must be recognized that a composite photograph is only exceptionally seen, as details will be present in one case and not in another, and the intensity of each evidence is very variable. However, that we may have prototypes of premature detachment we present these imaginary but graphic examples:

The woman may be asleep or concerned with her varied duties while in pregnancy or in labor. Suddenly she feels an abdominal discomfort, indefinitely located or limited to the uterus. She becomes dizzy, and soon regains her equilibrium. Nausea may or may not be present. If she is in labor the contractions increase in vigor and pain persists in the intervals between contractions. Again, after a period of unrest, all symptoms may subside and in the course of time labor begins. If the bleeding is sufficiently ample, whitening of the mucous membranes appears, and even the skin is blanched to a degree. The fetal movements may be clearly perceived, but finally they disappear. The physician comes; he corroborates the evidence of an anemia by repeated blood examinations, notes some tenderness, and if the small hemorrhage is restrained within the bounds of a uteroplacental cavity, he may note the the uterine protuberance—the accessory tumor. If the separation is limited the fetal heart tones may be variable, from normal to marked irregularity, and rapid; if there is an extensive separation the fetal heart is inaudible and fetal movements will have ceased. The uterine consistency may be little altered. After a variable period there may be a pinkish serous discharge, followed later by the escape of dark old blood, even black firm clots. The temperature falls, the amount depending upon the volume of blood loss; in this type of separation the blood loss is commonly not great. Also depending upon the blood loss, the blood pressure may be depressed. Urinary examination may not show any abnormality, or there may be some evidence of an acute nephritis—traces of albumin, few casts. This is the picture in mild to fairly severe cases, which may result from trauma, from purely localized pathology of the uteroplacental union, or some toxemias of lesser severity. In contrast to these manifestations we have the other extreme:

The patient may have had a known nephritic involvement, with some hypertension—or this may have been unobserved. Without premonitory signs she is seized with an agonizing pain, described perhaps as a bursting pain. She collapses and may be unconscious. The mucous membranes are without color, the skin dank and of waxy whiteness. She may be in deep shock. The pulse rate is very rapid and of poor quality. Serial blood counts show a high grade anemia. Whatever the blood pressure may have been prior to the attack (hypertension), it is now distinctly depressed. The physician finds the uterus symmetrically enlarged or showing marked deviation in contour. The patient, when revived, tells of tumultuous fetal movements for a few moments, then quiet. The malposition of the baby may be discovered if the uterus is sufficiently relaxed, but in other cases the tension is so great (tetanic contraction) that nothing in utero is palpable. Tenderness pervades the whole uterus, especially over the placenta. Appalling external hemorrhage may appear or there may be no showing for a protracted period. Finally, there is a profuse discharge of the serous fluid (blood serum extruded from the clot) sometimes of such quantity that it is mistaken for liquor amnii. Later, slight to profuse discharges of old black blood interspersed with old clots are in evidence. Urinalysis usually shows definite albuminuria, casts erythrocytes and hemoglobinuria, varying with the intensity of the toxemia.

So far as now known, uteroplacental apoplexy does not offer any clinical intimation of its existence. It is entirely theoretic but we may predicate its existence if

symptoms are out of all proportion to the amount of blood loss. As the placenta of this group is almost invariably entirely degenerated, the violent onset is accompanied by especially sharp uterine turmoil —pain to an extreme degree, and often, though not invariably, an excessive rigidity of the organ. One may be justified in considering that the placenta has been completely severed from its attachment. The hemorrhage of this form of toxemia is rather less than in other types. The bleeding is characterized by the sudden outpouring, then a remarkably quick coagulation; the later external bleeding may be negligible, hardly spotting, and rarely will there be a postpartum hemorrhage. These symptoms are in sharp contrast to the external gushing which may dominate the picture where a severe injury caused the separation. Couvelaire states that vascular lesions and hypertension are not necessarily a part of the trouble. Shock is often present. The correlation of a leucocytosis (polymorphonuclear leukocytosis) of the maternal circulation and its presence in the uterine and placental tissues deserves an intensive study. At the present time we may not recognize the existence of this condition (apoplexy) unless we inspect the uterus during a cesarean section or on the postmortem table.

The third stage of labor will offer conclusive corroboratory evidences of the correctness of a diagnosis of ablatio of every type, or entirely negate the thought. The expulsion of old black blood and old clots with the fetus and placenta is so constant that their absence is indicative of a lateral previa.

DIFFERENTIAL DIAGNOSIS

The diagnostic difficulties in the interpretation of the phenomena included under the broad caption of premature separation of the normally situated placenta must be appreciated when the range spreads from those minor abnormalities which are recognizable only by inspection of the secundines, through those which give extremely vague and transitory discomforts, on to those with marked symptomatology and high lethal crises, to uteroplacental apoplexy. J. Nevins Hyde, the eminent dermatologist, maintained that the mutability of syphilitic evidences was so great that there were few diseases which it did not resemble. In the same manner, the clinical expressions of ablatio have such vagaries that they may resemble other hemorrhagic disorders, or even simple alien manifestations.

Dizziness, faintness or syncope are inherent accompaniments of all losses of blood. In the past, and even today, too much stress is laid upon their occurrence as normal (!) reflections of the cerebral instability of the pregnant woman. By the same token, nausea and emesis are too lightly held to be features characteristic of the pregnant woman's gastroenteric unrest. Their occurrence demands that the physician shall not cease search for the basis for their inception. Too often the case reports demonstrate the quandary of the physician until he is enlightened by the external bleeding. In such cases sooner or later the blood picture will reveal the fact of a progressive anemia.

Placenta Previa. In previa the first sign of trouble is vaginal bleeding, but it may be one of the last evidences of ablatio. Both the hemorrhage of previa and that of ablatio *may* result from some seemingly trivial trauma. The uterus in previa is never abnormal in contour, unless because of malpresentations, and never is it increased in size. In ablatio the contour is frequently disturbed by concealed hemorrhage and if this is extensive the uterus is invariably increased in bulk. A vaginal examination will permit the discovery of the low placenta, and the textural changes incident to a previa. The placenta in premature detachment is never palpable. As previously stated, the line of demarcation between a placenta which approximates the area of the retraction ring, and one which definitely dips into it may not be

clinically demonstrable: if the lower border of the former separates as the latter (a high lateral previa) inevitably must, the hemorrhages may hardly be differentiated, for both will be without accompanying discomfort. As the appropriate treatment of both is the same, the distinction between low placental separation and high lateral previa is of no importance. Inspection of the extruded secundines will permit one to measure the distance between the chorionic opening and the placenta; if short it probably is a previa, if longer, ablatio.

Uterine Rupture. Rupture of the uterus generally takes place late in labor at a time when a few placental separations may occur. The complete dehiscence with the extrusion of the fetus into the abdomen hardly permits confusion of one with the other. However, incomplete destruction of continuity may cause confusion in diagnosis. The labor is prolonged, with gradually increasing pain between contractions, and more acutely perceived with them. The round ligaments, long before the accident takes place, are tender to the touch, tense and swollen. With rupture, pain greatly diminishes. Pain is almost constantly located suprapubically, and an obstructed labor is usually the cause. The pain of ablatio is high in the uterine wall, localized or diffusely perceived by the patient. In both, external bleeding may occur unless dammed back by the presenting part. If the uterus is completely torn through the escape of the fetus into the abdominal cavity, and sharp retraction of the organ occurs there is no difficulty; in the incomplete forms the uterus rarely increases in size, while in ablatio distention is noted.

Acute Polyhydramnios. The rapid accumulation of liquor amnii, usually during a period of days, sometimes in a few hours, never produces hemorrhage during the process. The uterus always is either piriform or spherical. Measures should be taken to prevent a rapid escape of the fluid, for there is danger of placental separation from sudden contraction and retraction.

PROGNOSIS

The writer has expressed his conviction that generic ablatio comprehends at least four, if not more, distinct maladies. Each has its specific etiology and pathology with placental separation and hemorrhage common to all. Adventitious clinical signs and symptoms are *seemingly* possessed by all, but future investigators will probably evaluate them properly, producing a separate symptom complex for each. Three of these etiologic types have certain pathologic identifications, local or systemic, which permit a certain degree of differentiation. These three may have their onset precipitated by trauma. Injury alone *may* induce the catastrophe in the absence of local degenerations. Each type *may* be evinced by trivial signs, by marked reactions, or by most tumultuous unheavels. In our ignorance of fundamental principles there is no common standard for classification of types, of their symptom equivalences or contrasts, of the enumeration of the relative values of methods of treatment *for each*, or a means for the calculations of the respective mortality rates. All data must, more or less, be summarized collectively. Migraine, eye strain, and penetrating gunshot wounds of the brain have a common symptom—headache—but who would group these together for therapy or present a common mortality rate for the three. Any plan for the comparative study of mortality rates is fraught with inconsistencies, although certain trends are clear.

Irving has most graphically portrayed the influence of two of the etiologic factors. The Boston Lying-in Hospital had 224 instances of nontoxic ablatio with eight maternal deaths—3.5 per cent; 129 toxemic separations with ten deaths—7.7 per cent. It is not known how many Couvelaire apoplexies were among the latter, but we do know the mortality rate is materially higher than for ordinary toxemias. These same 353 cases were regrouped into external and internal hemorrhages; there were 234 examples of the former with four

deaths—1.7 per cent; 119 of the latter with fourteen deaths—11.8 per cent. Of the latter, Irving states that in "all but two of our cases of internal hemorrhage, there was some visible bleeding at some time." We question the advisability of this distribution, for a concealed hemorrhage is never patent. We would reiterate that the external flowing, whether large or small, is no criterion of the amount of internal accumulation. The delay in recognizing an absolutely concealed case must contribute to increased death rates.

Table VII

MATERNAL MORTALITIES IN ABLATIO PLACENTAE

Spontaneous Births and Conservative Management

Authority	No. of Cases	Deaths	Rate Per Cent
Weymeersch-Snoeck	853	56	6.6
Davis-McGee	330	18	5.5
Irving	204	1	0.5
De Snoo-Streink	214	11	5.1
Le Lorier	56	1	1.7
A. F. Maxwell	47	0	0
Solomons	25	1	4.0
Bland-Rokoff	414	16	4.1
Totals	2,143	104	4.9
Spanish Windlass with Rupture of the Membranes and Tight Cervicovaginal Tamponade			
Polak	16	1	6.2
Irving	16	0	0
Heffernan	7	0	0
Totals	39	1	2.6

The tonicity of the uterine wall is of some value in determining the maternal risk. A firm wall is more prone to react to stimuli since firmness tends to inhibit retention of an undue amount of blood. When relaxation is present the converse may be true. Of the 306 cases collected by Goodell and the writer, the status of the uterus was given in eighty-six; there were twenty-two deaths among the sixty-six women with tense uteri—33.3 per cent—and nine deaths in the twenty with relaxed uteri—45 per cent.

Irving's tabulation of mortality rates as influenced by intervention is most enlightening, for it utterly shatters every rule that all placental detachments be managed by radical or polypragmatic practices, such as routine cesarean section. Irving characterized the period when accouchement forcé was rampant as the "dark age" of modern obstetrics; the promiscuity with which cesarean sections were performed for nonsensical or spurious indications may be added to the reason for such a "dark age." In the heyday of cesareans for eclampsia

Table VIII

MATERNAL MORTALITIES IN ABLATIO PLACENTAE

Results from Cesarean Section

Authority	No. of Cases	Deaths	Rate Per Cent
Le Lorier	4	1	25.0
Weymeersch-Snoeck	227	47	21.0
Maxwell	8	1	12.5
Irving	99	11	11.1
Willson	21	4	19.0
Brodhead	8	3	37.5
Williams	10	3	30.0
Fitzgibbon	4	1	25.0
Siegels	11	2	18.2
Davis-McGee	29	4	13.8
Bland-Rokoff	107	12	11.2
Goethals	39	6	15.4
Totals	567	95	16.8

the writer repeatedly asked the opinion of general surgeons regarding the advisability of an abdominal operation on a patient whose kidneys were grievously injured by an acute nephritis, whose liver was in gross dysfunction from some lethal poison. The consensus of opinion was, "never," unless the necessity was so great that no other recourse were possible. Obstetric attendants have been slow in learning this aphorism. This has a direct application in connection with the treatment of ablatios. Irving puts it, "The most remarkable argument advanced by the proponents of cesarean section is that it affords an opportunity to perform a hysterectomy . . . The logic is not apparent which compels

one to perform an operation with a 20 per cent mortality, so he may convert it into another with twice the death rate." Tables VII to XI show the mortality rates under various conditions as presented by different authors.

TABLE IX
MATERNAL MORTALITIES IN ABLATIO PLACENTAE
Results from Supravaginal Hysterectomy

Authority	No. of Cases	Deaths	Rate Per Cent
Welz	3	1	33.3
Willson*	21	10	47.6
Fitzgibbon	3	2	66.7
Le Lorier	2	1	50.0
Maxwell*	1	1	100.0
Davis-McGee	6	0	0
Polak, Burgess, Bartholemew	3	0	0
Holmes*	1	0	0
Totals	40	15	37.5

* All proved cases of Couvelaire's uterus.

TABLE X
MATERNAL MORTALITIES IN ABLATIO PLACENTAE
Results from Pelvic Operative Delivery—Radical Treatment

Type of Interference	No. of Cases	Deaths	Rate Per Cent
Radical Treatment, Bland-Rokoff	284	38	13.4
Pelvic Operations, Irving	50	6	12.0
Brindeau-Lantuejol	18	2	11.1
Breech Extraction*	28	0	0
Craniotomy*	9	0	0
Forceps*	152	24	15.8
Version-extraction*	33	5	15.2
Vaginal cesarean section*	9	4	44.4
Maxwell	1	1	100.0
Hystereurynter*	57	7	12.3
Maxwell	10	2	20.0
Totals	651	89	13.7

* Adapted from Davis and McGee. Bland-Rokoff reported six deaths after eleven attempts at forced dilatation—54.5 per cent.

The mother may die as the result of blood losses, largely from toxemia, from shock, and from sepsis. In the best of hands sepsis must destroy a few mothers, particularly where antecedent manipulations have preceded entry to the hospital. The fetus may die from asphyxiation, possibly from hemorrhage through the torn placenta,

TABLE XI
COMPARATIVE FETAL MORTALITIES IN ABLATIO PLACENTAE
Resulting from Conservative Management, Cesarean Section and Radical or Operative Treatment

Methods	No. of Infants	Deaths	Rate Per Cent
Conservative Management			
Irving	241	102	42.3
Maxwell	40	10	21.3
Solomons	29	8	27.6
Bland-Rokoff	414	251	60.7
Weymeerch-Snoeck	853	522	61.3
De Snoo-Streink	214	166	78.0
Totals	1,791	1,059	59.1
Cesarean Section			
Irving	100	54	54.0
Maxwell	9	2	22.2
Bland-Rokoff	107	80	74.7
Weymeersch-Snoeck	227	175	70.7
Totals	443	311	70.2
Radical or Pelvic Operative Treatment			
Irving	16	15	93.7
Maxwell	10	7	70.0
Bland-Rokoff	284	207	73.0
Totals	310	231	74.5

certainly from toxemia, and prematurity. Goodell stated that detachments were responsible for the premature interruption of pregnancy in 50.5 per cent of all cases. Of 200 cases collected by the writer, in 157 the period when the symptoms appeared was stated: six were in the fifth month, four in the sixth, twenty-nine in the seventh, sixty-two in the eighth, and fifty-two in the ninth or at term. In other words, 64 per cent were premature. According to Irving forty-five premature terminations occurred among the 357 infants born—12.6 per cent.

TREATMENT

It is sufficiently evident that generic ablatio, comprising four or more unques-

tioned puerperal diseases, each of which deports itself with varying clinical intensity and different symptomatology, cannot have a routine management. There must be individualization of each case, and the method most suitable should be selected. Minor cases require the least interference compatible with the welfare of the mother. Fulminant ablatio requires an intervention which will decrease the gravity of risk, not an operation which will augment it. It would be utterly preposterous to maintain that cesarean section has no place in the management of certain placental detachments, but the suitability is restricted to a limited field. The nationally held notion that the abdominal route is the only solution is as false a premise as in eclampsia.

Introduction. The first prerequisite is that the laity should be educated to the precept that every little malaise may have its serious portent. They should call a physician early. And he should not rest until he has eliminated any and all possible underlying causes. Weymeersch and Snoeck state that intervention prior to a ten hour period carries a mortality of below 27 per cent; after that it rises to 40 per cent. Secondly, every patient must be given supportive treatment according to her needs. Blood transfusions are of vital necessity when the blood losses have been great. As a temporary expedient the parenteral or rectal administration of decinormal solutions may turn the tide. In the distinctly toxemic patient the salines and Ringer's solution will be of advantage in aiding elimination; glucose solutions are advisable in shock. Morphia in fractional doses is invaluable as an adjuvant where much blood loss has occurred, for the purpose of quieting the highly nervous woman. As the fetal mortality is exceedingly high at best, the fetal contraindication to the use of morphia is not valid. Finally, one must select that type of interference which guarantees the greatest safety for the mother. Above all things, select the method which shall be the primary, as well as the sequential pursuit. Selecting one method and then turning to another is an obstetric blunder.

Conservative Measures. The expectant treatment has various modifications, introduced by various clinicians, but all have a common purpose in that drastic measures are entirely eliminated. The keynote of all variants is expectancy: a nurse must be in constant attendance; there must be frequent recording of pulse, temperature, blood pressure. The character of the contractions, changes in the nature of the pains, and tenderness of the uterus are noted. Frequent observations and palpations ascertain changes, if any, in uterine contour and size. The amount and appearance of the escaping blood are observed. The consensus of opinion is that the membranes are to be ruptured artificially, particularly if the uterus is contracting. In the absence of uterine activity, or even with its presence, fractional doses of a pituitary extract are given; nasal administration is more desirable as the plug may be removed promptly, if indicated. Any sort of massage of the womb is absolutely prohibited.

There is fair unanimity that spontaneous labor shall be awaited, and forceps employed only on definite indication when the head has descended deeply into the pelvis. Some would modify this by employing instruments as a prophylactic measure, but *high forceps should not be tolerated.* If the breech presents, as it will in about double the normal frequency, manual aid should be given or extraction, on indication only, after dilatation has been completed. During the hours of waiting such supportive treatment as is expedient should be administered. Some will routinely give saline solutions by clysis, even subcutaneously. Blood transfusions may be indicated in exceptional cases. This method is appropriate for at least 60 per cent of all types of premature detachment. The ultra-conservative physician will obtain happy results in a larger proportion than given above.

Some writers, by implication at least, would limit this method of treatment to

spontaneous labors alone, while others would include minor operative interferences, and others, apparently, would include forceps in the non-operative group, as they call routine forceps termination in normal labor as "spontaneous." For the more seriously compromised, the tampon and Spanish windlass treatment would be considered an extremely conservative measure as the results are nearly ideal. The use of the tampon was the time honored treatment for "accidental hemorrhage" in the Rotunda Hospital for over 100 years and was discarded by Bethel Solomons shortly after he assumed the mastership, as he left the mere rupture of the membranes, with indicated supportive measures, fulfilled every purpose. John O. Polak was so successful with the tampon combined with the Spanish windlass that Irving and Heffernan adopted the method to evade the cesarean operation. The technique is so simple that it is worthy of emulation. We must point out that the use of the tampon (or hystereurynter) carries a great inconsistency: every writer stresses the fact that absolutely concealed hemorrhages are more fatal than patent ones. Any type of plugging of the cervix or vagina converts an overt hemorrhage back to a totally concealed one. We have always maintained that the entirely concealed hemorrhage was more dangerous as it permitted procrastination before treatment could be based on a positive diagnosis. The paradoxical use of the tampon would seem to confirm this opinion.

Hystereurysis. The rubber bag acts similarly to the tampon, but has the greater advantage in that there is more certain stimulation of the uterus and it will more surely arouse contractions, consummate dilatation more quickly, and more definitely prevent external bleeding. The one objection is that experience has taught that the intra-uterine bag is more prone to be followed by a septic death. In fact, sepsis vies with hemorrhage as a cause of the demise. The seeming ill effects (12 to 20 per cent death rate) probably would be largely reduced if it were combined with the Spanish windlass. The membranes must be ruptured before the bag is introduced. However, on the returns, it would be preferable to use the tight tamponade.

Extraction of the Fetus. All statistics demonstrate that the best results obtain when spontaneous labor occurs. Therefore, it is desirable that no attempts at delivery should be assayed unless there is a clear indication. Those who practice the tenet that routine forceps are within the domain of spontaneous labor should discard the procedure for cases of ablatio. The same comments apply to extraction of the breech. High forceps connote an extraction through a partially dilated os, and should never be employed. Version carries its own risks, for it may cause an additional separation, just as its use may produce a primary separation. Version should only be done in transverse presentations, and on a *living baby*. On the dead, in early prematurity, or in the dying, decapitation or embryotomy should be done. The most remarkable feature elicited from a perusal of the literature is the paucity of cases delivered by craniotomy—in a condition with a fetal mortality of from 60 to 90 per cent. In the collection of the writer (1901), covering a period when craniotomy vied in frequency with forceps in some hospitals, there were but three craniotomies mentioned in 200 cases of detachment. In the recent literature only nine women had craniotomized babies. Times were when it was taught that forceps on a dead fetus was the height of violation of sound obstetric principles and the use of standard sized forceps on a premature fetus was a transgression. Yet there were twelve craniotomies recorded in an array of over 4,000 cases of a complication in which at least 2,400 dead feti were delivered, due to prematurity or asphyxiation or both! Under appropriate conditions cranioclasis is infinitely safer than forceps. We hold no brief for the abhorrent destruction of the living fetus, but we protest the esthetic fastidiousness which dictates an

irrational forceps operation on a dead baby when a craniotomy would be more scientifically correct and less dangerous to the mother. Cathala of Paris is the only one consulted who has dictated a similar teaching as the author. Vaginal cesarean section has a very small place in the operative treatment of placental detachments—the mitigating circumstances are very few. The blood bathed field seriously handicaps the technique.

Cesarean Section. This operation has been lauded the past years as the panacea for nearly all cases of placental separation by some writers of collated statistics who did not properly digest the facts. On the other hand, authorities who summarize wide experience demand that the procedure be limited to the few cases where other recourses are impossible.

Irving writes: "The woman with this form of internal hemorrhage [placental detachment] is not only handicapped by acute blood loss, but she is often the victim of shock—in three-fifths of the cases toxemia is present . . . accompanied by a partial or complete suppression of urine. It would be difficult to envisage a more dangerous basis for such a surgical operation as cesarean section, a procedure in itself of considerable magnitude and often complicated by further hemorrhage. All judgment should be against it, provided there exists a safer and less radical means of escape."

Cathala states: "Conservative cesarean section is rarely indicated." Alice F. Maxwell declares: "The high maternal mortality following abdominal delivery indicates that surgical measures for the treatment of concealed hemorrhage have been universally unsatisfactory."

The orthodoxy of Irving and Maxwell may be corroborated by an analysis of several tables. The combination of Tables VIII (conservative management) and X (radical treatment) reveal that 2,794 women who were afflicted with some type of ablatio were delivered through the birth canal with 193 deaths—6.9 per cent. If these same women had been cesareanized with the death rate shown in Table IX (16.8 per cent) there would have been 469 deaths—an increase of 276.

The Fetus. The total vaginal births in Table XI amounted to 2,101 with 1,290 deaths—61.4 per cent. If this rate (61.4 per cent) were applied to the women vaginally delivered there would have been 1,715 fetal deaths. If the cesarean rate (70.2 per cent) in the same table be used, 2,061 feti would have perished—an increase of 346. In this hypothetical computation the performance of cesarean section would have sacrificed 276 additional mothers that 346 feti might be exterminated. Cesarean mortalities in placenta previa have already been noted. Here are others which would corroborate the stand of Irving and Maxwell. In 1929, 174 hospitals reported 3,264 cesareans with a mortality of 8.95 per cent in contrast to a puerperal mortality rate of 0.7 per cent for those who were otherwise delivered. *These cesarean deaths constituted 28.0 per cent of all puerperal deaths.* One hundred and twenty-six hospitals reported 2,909 cesarean sections with 292 fetal deaths—a rate of 10 per cent. The death rate of infants (stillbirths and natal) otherwise born was 7.2 per cent. The cesarean deaths constituted 4.5 per cent of all fetal demises. The portent is so ominous that it behooves the obstetric teachers to inculcate conservatism, not only in premature detachments, but in all other directions.

The consensus of opinion is that the operation should be restricted to those cases where these conditions obtain: (1) a fetus near term and alive at the time of operation; (2) a contributory indication such as material pelvic contraction which reasonably would dictate the operation without a detachment (disproportion is infrequent as prematurity is present in about one-third of all cases); (3) a gross anomaly of the soft parts, as strictures, or true cervical rigidity—a relaxation of the cervix is the rule, not an exception; (4) no prior attempts at vaginal interference of any sort; (5) unless the patient is in good condition, with minimal hemorrhage, low

grade of toxemia, and no shock, recuperative measures before the operation, including blood, saline, glucose, Ringer's solution, and general stimulation as required. The question whether a classic or low cervical operation shall be done depends entirely upon the reliance of the operator on his technical skill.

Hysterectomy. The removal of the uterus is not an essential detail of the treatment. The policy of such a course when a true Couvelaire uterus is found is based entirely on false premises. Such a uterus rarely bleeds; the infiltration of blood does not spell a dead uterus—if the woman recovers all will be absorbed. The ablation of the uterus only is justifiable when there is an uncontrolled hemorrhage from atony, in the presence of a sepsis, or the danger of it is there from antecedent attempts at delivery.

The danger of cesarean section is graphically portrayed by Irving. Blood transfusions were roughly two and a half to seven times the frequency for sectioned cases as for those vaginally delivered. Toxic apoplexy, in fact all types of ablatio, is a fortuitous circumstance which will not recur. It is not right to subject patients to an operation (cesarean) which carries a definite hazard of uterine rupture in subsequent labors, or demand that all later births be sectioned to evade the risk. Neither is it justifiable to sterilize by hysterectomy on specious reasons, thus robbing patients of potential children. Keller states: "Eleven of eighteen women who were observed later became pregnant, and there were sixteen pregnancies with fourteen living children, and no recurrence of uteroplacental apoplexy."

Manual Dilatation. The circumstances are so exceptional for the manual dilatation of the cervix, and the conditions must be so characteristically present, that this procedure need no further comment here.

The Third Stage. It is usual for the placenta to be expelled with the fetus when the severance is complete. If the placenta is partially detached, the whole serotina being involved, the third stage is completed without difficulty in most instances. In some cases due to local pathology of the basalis there may be a necessity of using a Credé, and occasionally a manual removal will be necessitated. Every precaution should be taken to conserve blood losses in this period. A small postpartum hemorrhage in a woman already anemic may be disastrous. Every attendant who must assume the care of a woman with a detachment should know the technique of uterovaginal tamponade. It is wiser for the casual operator to tampon too often rather than to neglect it where it might be a necessity.

CONCLUSIONS

1. The presumptive evidence is nearly conclusive that there are at least four etiologic factors involved in placental separations: traumatic, inflammatory or local degenerative alterations of the serotina, toxemias of varying intensities, and a Couvelaire uteroplacental apoplexy. Real progress in knowledge will come only when these divers types are studied separately. Any attempt to apply a discussion which shall cover the four types indiscriminately merely leads to chaos.

2. The degree of separation of the placenta will be found of less importance than the amount of blood lost. It is notably recognized that uteroplacental apoplexies do not ordinarily have a great excess of bleeding. The toxemia is the serious complication which destroys.

3. Conservative treatment will bring the surest success, vaginal operations second; and cesarean section third. Hysterectomy doubles the mortality of any form of abdominal delivery.

5. The combination of a firm vaginal tamponade with the Spanish windlass apparently promises the greatest chance of a happy termination over all other methods where operative work is deemed essential.

6. As prematurity and fetal death prior to hospitalization play such havoc, everything should center upon saving the mother.

7. All women with placental detachment require a reliable hospital service.

THE PREVENTION AND TREATMENT OF ECLAMPSIA*

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THE cause of eclampsia is still unknown, but considerable data indicating a markedly abnormal physiology associated with or perhaps causing the condition have been collected and partially interpreted. The result has been an appreciable reduction in the mortality, due in great part to the treatment which is now directed at improving or correcting the deranged physiology of the various organs and systems involved in the disease. There has also been a constant decrease in the number of patients with eclampsia due to prenatal care.

Our definition of eclampsia is as follows: *clinical*—as the occurrence of convulsions and/or coma in a pregnant or recently delivered woman if associated with hypertension, albuminuria, or edema; *pathologic*—the presence in the liver of periportal hemorrhages and necrosis, of anemic infarcts, or thrombosis of the portal vein or its branches in a pregnant or recently delivered woman if associated before death with any or all of the symptoms or signs previously described.

We believe that the changes in blood and plasma volume are also characteristic of the disease and that the final diagnosis should be based on the clinical course and laboratory findings. The periportal hemorrhages and necrosis which are given as a pathognomonic lesion of eclampsia have been found in a few pregnant patients who had none of the clinical findings of eclampsia. This periportal lesion, however, is peculiar to pregnancy. Furthermore, patients who die ten days or more after the convulsive seizure have normal livers. The most reasonable explanation is that the convulsions and coma can occur in the following types:

1. Eclampsia, characterized by excessive weight gain and/or edema, albuminuria, hypertension, and the various cerebral, visual, gastrointestinal, and renal symptoms and signs.

2. Hypertensive encephalopathy characterized by hypertension, albuminuria, and little or no edema. The so-called "dry eclamptic" probably belongs to this group.

We have studied several patients belonging to the latter group, but the chief difficulty in identifying them is that there is no reason why eclampsia cannot be superimposed on an arterial hypertensive disease. It will require the study of many more cases than we now have to prove this classification beyond question. However, everyone who has studied many cases of eclampsia has noticed differences in response to treatment, especially to sedative drugs. There are many other points of difference, but the lowest maternal mortality for eclampsia is usually achieved by delivery or early fetal death, whereas in hypertensive encephalopathy, delivery is of less importance and the lowest mortality results from the use of large amounts of sedative drugs.

The separation of convulsive toxemia of pregnancy into two types is somewhat academic because our treatment at present is identical. Furthermore, it is difficult during the acute phase of the disease to classify it properly. However, because progress can only be made by attempting to clarify various conditions and diseases, the classification is adhered to.

We have, for a number of years, grouped the various signs and symptoms as follows:

1. *Non-Convulsive Toxemia:* Pre-eclampsia, essential hypertension, vascu-

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lar-renal disease, glomerulonephritis.

A. Edema (weight), proteinuria, hypertension (individual).

B. Cerebral symptoms and signs—headache, dizziness, restlessness, amnesia, increased pulse and respiratory rate and fever.

C. Visual symptoms—diplopia, scotoma, decrease in vision, and amaurosis.

D. Gastrointestinal disturbances—epigastric pain, vomiting, jaundice.

E. Renal disturbances— oliguria, anuria, hematuria.

II. *Convulsive Toxemia.*

A. Convulsions—coma.

Non-convulsive toxemia cannot be prevented, but the doctor who practices intelligent prenatal care will appreciate the importance of group A signs and will prevent the onset of the symptoms and signs in groups B to E by the use of diet, proper elimination, and suitable drugs. Likewise, the appearance of any or all the findings in the latter groups indicate that eclampsia is imminent and that more drastic measures must be instituted.

Edema. Slight pitting edema of the ankles is a common finding in late pregnancy. It is due in great part to an increased venous pressure, caused by pressure of the uterus on the common iliac veins. Edema of the legs or other parts of the body is abnormal. Marked edema is quite often the first sign of pre-eclampsia and in conjunction with the other signs is found in 40 per cent of the mild pre-eclamptics and in 66 per cent of the severe, in contrast to essential hypertension where the figures are 3 per cent and 14 per cent and in vascular-renal disease where they are 29 per cent and 27 per cent, respectively. Approximately 75 per cent of eclamptic patients have marked edema.

The edema in our patients is not due to a hypoproteinemia. We have been determining serum protein concentrations since 1925 and have a large series from normal and toxemic patients. Our average serum protein concentration in normal pregnant women is 6.4 Gm. per cent with a standard deviation of 0.4 Gm. per cent; in pre-eclampsia 6.0 Gm. per cent; in vascular-renal groups 6.6 and in eclampsia 6.7 Gm. per cent. Our determination of the colloid osmotic pressure of pregnant and toxemic patients indicates that the osmotic pressure is always above the edema level. The determined and calculated osmotic pressure checks within the experimental limit, indicating that the serum albumin and globulin are normal in their composition. We believe all evidence to date indicates that the edema in most pre-eclamptic and eclamptic patients is due to changes in the permeability of the capillary and cell wall.

Weight. Many patients have abnormal gains in weight, which can only be due to retained water, long before they have demonstrable edema. There has been considerable discussion as to the relation between excessive gain in weight during pregnancy and the occurrence of toxemia. Siddall and Mack report that similar excessive or too rapid gains in weight may occur in both normal and toxemic pregnancies. One criticism of their work is that they did not correlate the type of toxemia with the gain in weight. The pre-eclamptic and eclamptic patients usually gain excessively or too rapidly. The average gain in weight in normal pregnancy from various reports is 9 Kg., range 7 to 11. Our normal patients who were followed from twenty-seven weeks to term gained 8.1 with standard deviation of 1.5 Kg., those followed from twenty weeks to term gained 12.4 with a standard deviation of 3.7. If both groups are combined, the average is 9.7 with a standard deviation of 4.3 kilo. Furthermore, during the prenatal period, neither doctor or patient knows what the future gain in weight will be. Therefore for many years, the experienced doctor has calculated the weekly or monthly gain at each examination and been guided in his treatment by this information. The consensus of opinion is that the weight gain of the last

half of pregnancy ranges from 280 to 500 Gm. per week with an average of 400 Gm.

The average weight of the fetus, placenta, and amniotic fluid amounts to 4,200 Gm. and the necessary weight gain due to the physiologic changes of pregnancy (uterus, blood volume, breasts, etc.) amounts to a maximum of 2500 Gm., giving a total of 6.7 Kg. Since 1936 we have been insisting on a weight gain of not to exceed 300 Gm. per week, the total gain not to exceed 8 Kg. One to 3 gr. of thyroid extract in addition to diet has been used since 1937 to aid in preventing excessive gains.

Brown and I have shown that the total weight gain and gain per week are related to the type of toxemia. Twenty-nine per cent of the pre-eclamptics, 14 per cent of the vascular-renal, and 13 per cent of the essential hypertensive patients gained an average of 12 Kg. Seventy-four per cent of the severe pre-eclamptics, 49 per cent of the severe vascular-renal, and 23 per cent of the severe hypertensive group gained at a rate greater than 0.6 Kg. per week. Twenty-four per cent of the severe pre-eclamptic and 10 per cent of the severe vascular-renal patients gained on an average of 1 or more Kg. per week. Single period gains have been as much as 3 Kg. per week and with NH_4Cl, we have noted a 7 Kg. loss in one week. These excessive changes in weight must be due to alteration in the water balance.

Proteinuria. The usual qualitative tests reveal no protein in the urine of normal pregnant patients, but a quantitative determination will yield 0 to 0.3 Gm. per twenty-four hours. If a positive quantitative test for protein, which should always suggest toxemia, is found, the patients, since 1935, have been instructed to save the urine in a single container for twenty-four hours, measure it and bring a small specimen to the doctor. Quantitative determinations for protein, chloride and non-protein nitrogen are made. The total excretion of protein per twenty-four hours is usually less than 1.0 Gm. Generally speaking, as long as the proteinuria was less than 5.0 Gm. per twenty-four hours, the patient was observed at weekly intervals. However, the persistent excretion of more than 5.0 Gm. indicated the need for hospitalization because fetal death in utero due to placental infarction quite often occurred in the arterial hypertensive patient and eclampsia was imminent in the pre-eclamptic. The non-protein nitrogen determination as a measure of the nitrogen metabolism indicated that the protein intake ranged from 1 to 2 Gm. per kilo of body weight. The determination of chlorides was used as a check on the patient's diet. The NaCl excretion must be less than 3 Gm. per twenty-four hours to be of any value as a therapeutic measure in the treatment of edema and as a preventive against further increase in the blood pressure.

Proteinuria (two plus or more) was found on more than two occasions in the urines of 40 per cent of the mild and 88 per cent of the severe pre-eclamptic group; 26 per cent of the mild and 65 per cent of the severe vascular-renal disease group; and 13 per cent of the mild and 50 per cent of the severe essential hypertension group. Albumin forms the greater part of the protein found in the urine. The amount and duration of loss is never sufficient in pre-eclampsia to cause a hypoproteinemia. In severe vascular-renal disease, chronic glomerulonephritis, and nephrosis, the loss is quite often great enough and, especially, the duration of the disease is long enough seriously to lower the serum protein concentration of the blood.

Urinary Sediment. The Addis count indicates that the number of casts, erythrocytes, leucocytes, and epithelial cells is slightly increased in normal pregnancy and increased even more in the toxemias. The occurrence of an abnormal urine sediment indicates the need for repeated studies of the patient and a proper diagnosis of the disease. The occurrence for one week or more of red blood cells should suggest acute glomerulonephritis, pyelonephritis, nephro-

lithiasis, tuberculosis, or neoplasm. The presence of casts does not always indicate nephritis. This condition may be present but whenever albumin is present, a proper pH of the urine will result in the precipitation of some of the protein in the tubules, thus producing casts.

Hypertension. The normal blood pressure is 90 to 120 systolic and 60 to 80 diastolic. During pregnancy the blood pressure may increase to 121–129/79. A patient who has a systolic pressure of 130 or more on two occasions should be carefully watched. If the pressure is 140 or more, it is definitely abnormal, caused by vascular-renal disease, pre-eclampsia, or glomerulonephritis. An increase in the systolic pressure of 40 or more points, even though the final pressure is less than 140, must be regarded as abnormal.

Cerebral, Visual, and Gastrointestinal Disturbances. Headache, dizziness, restlessness, amnesia, increased pulse and respiratory rate, fever, diplopia, scotoma, decrease in vision, amaurosis, and vomiting are all due to cerebral anemia which may be caused by an edema of the brain or by a marked vascular spasm.

Patients differ as to whether cerebral or visual symptoms predominate. We regard the latter as the more serious. The loss of sight may be abrupt and, although the recovery is over a period of days, there is rarely any permanent decrease in visual acuity.

The epigastric pain is a local symptom and may be due to increased intestinal peristalsis or to the subcapsular liver hemorrhage. The jaundice is ascribed to liver impairment and indicates a very grave prognosis. Fever is most likely due to injury of the "heat center" in the medulla, resulting from cerebral anemia or from a possible, but not very probable, "eclamptic toxin."

The occurrence of these symptoms was always associated with hypertension and they were present in 4 per cent of the mild cases of pre-eclampsia, 3 per cent of the mild vascular-renal disease group, 2 per cent of the essential hypertension group, 50 per cent of the severe cases of pre-eclampsia, 49 per cent of the vascular-renal group, and 37 per cent of the essential hypertension group.

Renal Disturbances. The proteinuria, decrease in urine output, anuria, and occasional hematuria are probably due to an edema of the kidney tissue in pre-eclampsia and to arterial spasm and arteriolar sclerosis in the vascular-renal patient. Pre-eclampsia and eclampsia are characterized by an oliguria or even anuria. The urine contains a large amount of protein, but the concentration of salts and non-protein nitrogen is very low.

Convulsions and Coma. These are also due to cerebral anemia, resulting from edema in most cases, but also from arteriolar spasm in some cases.

Our treatment of non-convulsive toxemia of pregnancy is as follows:

1. Examination
   - Ambulatory—weekly or semi-weekly.
   - Hospital—The patient is weighed and a twenty-four hour urine examination for volume, quantitative protein, and chloride, and three determinations of the blood pressure are made daily.
2. Hypertension
   - Relaxation—adequate rest at night and 1 hour twice daily. As term is approached, more time may be spent in bed until all time is spent in bed.
   - Sedation—Phenobarbital (0.03–0.06 Gm. or ½–1 gr. three times daily). Potassium bromide (0.6 Gm. or 10 gr. three times daily). Luminal-sodium (0.3 Gm. or 5 gr. one or two times daily) subcutaneously in severe cases.
3. Elimination—Soapsuds enema and mild laxative as needed.
4. Excessive gain in weight—A diet composed of vegetables, fruits, lean meats which must be broiled, boiled, or roasted, eggs and 500

c.c. skimmed or buttermilk. No pie, cake, bread, butter, cream, gravy, soup, or table salt are used.

Pre-eclamptic—Salt-poor, protein 60 Gm., fat 30 Gm., carbohydrate 400 Gm., 2000 calories.

Eclamptic—Fruits and fruit juices with sugar. Limited five to ten days. 1200 calories.

5. Edema—A diet low in sodium and chloride. Watch water balance (weight). NH_4Cl in 1.0 Gm. gelatin capsules is given eight times daily for five days and repeated after a five day interval. If symptoms of cardiac decompensation are present, limit fluid intake to 500–1000 c.c.

6. Oliguria or anuria—Intravenous injection of 500–1000 c.c. of a 20 per cent solution of glucose two or three times daily. Occasionally 500–800 c.c. of a 30 per cent solution are necessary to produce a diuresis. If there is cardiac decompensation, 100–200 c.c. of a 50 per cent solution are used.

7. Proteinuria—Determination of the twenty-four hour amount as a prognostic guide. No specific treatment.

8. Cerebral, visual, and gastrointestinal symptoms—Sedation. Intravenous glucose. Delivery.

Renal function tests are of little value in the pre-eclamptic patients, but are of prognostic value in the other types of toxemia. Ophthalmoscopic examination is of value if pathologic changes are found, but normal findings do not rule out the gravity of the toxemia.

The occurrence of the following symptoms and signs indicate the need for hospitalization of the patient:

Pre-eclampsia: Possibility of eclampsia.

Hospitalize: Systolic blood pressure of 170 or more or increase of 40 mm. or more.

Appearance of marked edema, especially of face or abdominal wall (release of bound water).

Abnormal increase in weight with sudden increment of 2 or more pounds per week.

Proteinuria of more than 5.0 Gm. per twenty-four hours or concentration of 0.4 per cent or more (three plus test).

Appearance of cerebral, visual, or gastrointestinal symptoms.

Oliguria or hematuria.

Essential hypertension and vascular-renal disease: Eclampsia is uncommon. There is possibility of fetal death, especially after thirty weeks, because of placental infarction, retroplacental hematoma, or abruptio placentae.

Hospitalize: Increase of systolic blood pressure to 200 or more.

Proteinuria of more than 5 Gm. per twenty-four hours.

Marked edema.

Onset of symptoms.

The pregnancy should be terminated if any of the following symptoms or signs persist or increase despite treatment:

1. The systolic blood pressure is constantly 170 or shows a persistent daily increase.

2. The proteinuria always exceeds 5 Gm. per twenty-four hours or the qualitative test is three plus.

3. The weight gain exceeds 100 Gm. per day.

4. Marked edema suddenly occurs.

5. Cerebral, visual, or gastrointestinal symptoms arise.

6. Oliguria, anuria, or hematuria occur.

7. Jaundice develops.

8. The blood N.P.N. is 50 mg. per cent or more.

9. The pulse rate is 120 or more.

10. Edema of the lungs or cyanosis is present.

11. The blood shows an increasing concentration as indicated by an abnormally high or increasing hemoglobin, cell volume,

serum protein concentration or specific gravity.

Our results indicate that the careful medical management of the toxemic patient, if begun early enough, will usually prevent further increase in the severity of the symptoms and signs until the cervix is "ripe." This means that the cervix is effaced, soft and dilatable in the primipara or soft, and partly dilated in the multipara as determined by vaginal examination, and that labor can usually be successfully induced by rupture of the membranes. If contractions have not begun in twelve hours, ½ to 1 m. doses of pitocin should be given every thirty minutes until the contractions are occurring regularly at three to five minute intervals. The pre-eclamptic patient usually has an oliguria which minute doses of pituitrin exaggerate. Therefore, pitocin is suggested, but it is not completely free of the antidiuretic hormone and should be used with caution.

Table I
F. S. primipara, 19 years old, term 11/11/37

Date	Wt., Kg.	B.P.	Edema	Albuminuria	Remarks
8/5/37	63	135/80	++	0	NH_4Cl, 8 Gm. daily.
8/10/37	61	130/80	+	0	No salt or fat in the diet.
9/7/37	64	140/90	+	0	Hb. 11 Gm. per cent.
10/12/37	68	170/110	+	0	Complete rest, eclamptic diet, phenobarbital.
10/19/37	67	150/110	+	++	Increasing diet Serum protein 6.4 Gm. per cent.
11/2/37	69	170/120	+	+	Hospital. Ophthalmoscopic exam. normal.
11/3/37		160/100	+++	++	Rupture of membranes.
11/4/37		155/100			Delivery 2,670 Gm. baby.
11/15/37		140/90	0	+	U. C.—75 per cent. U/B—32.
11/18/38	55	110/70	0	0	U. C. 105 per cent. U/B—38.
12/12/39	57	120/80	0	0	U. C. 90 per cent. U/B—36.

The patient who does not respond to treatment or has been neglected is treated by rupture of the membranes and/or the insertion of a bag if the cervical canal is less than 2 cm. long, or, if there is no effacement and dilatation, by cesarean section under local anesthesia. From 1931 to 1933, 16 per cent of our toxemia patients were delivered by cesarean section with a fetal mortality of 12 per cent for fetuses weighing over 1500 Gm. For 1936 to 1938, 11 per cent were delivered by cesarean section and the fetal mortality was 4 per cent. The incidence of cesarean section in pre-eclamptic patients is 9 per cent and in the vascular-renal 20 per cent. These figures are still too high. The latter high figure is due in great part to a termination usually before term (unripe cervix) and need for tubal ligation.

Table II
S. W.—primipara, 21 years old, term 2/16/37

Date	Wt. Kg.	B.P.	Edema	Albuminuria	
10/15/36	57	120/80	0	0	Hb. 12 Gm. per cent.
10/31/36	58	140/90	0	0	Ophthalmoscopic exam. normal. No fats in diet.
1/5/37	62	160/110	+	0	Rest one hour twice daily. No salt in diet.
2/2/37	62	180/110	0	0	Complete rest in bed. Eclamptic diet.
2/16/37	62	210/120	0	0	Hospital
2/17/37		170/95	0		Rupture of membranes. Pitocin induction.
2/18/37		160/95	0	++	Normal delivery—3,545 Gm. baby.
2/24/37		185/115	0	+++	Urea clearance—85 per cent. U/B 50.
10/26/37		140/95	0		
3/21/38	51	153/95		0	12 wk. preg. Opthalmoscopic exam. early retinal sclerosis.
4/2/38		130/90		0	Hysterotomy and tubal ligation.
10/10/38		150/90		0	Urea clearance 79 per cent. U/B 30. S.P. 7.5.
10/5/39	53	140/90	0	0	Watch weight.

The case outline for F. S. (Table 1) is an example of pre-eclampsia. The abnormally rapid gain in weight, edema, hypertension and albuminuria are typical. The normal hemoglobin and serum protein concentration, normal ophthalmoscopic findings, and low normal urea clearance after delivery and normal one year later are the usual findings. Some of the changes in the signs seem marked but the patient was seen weekly and if any abrupt changes had occurred, she would have been hospitalized at once. We have learned to regard grad-

ually progressive changes with suspicion but not with undue alarm.

The case outline for S. W. (Table II), is an example of essential hypertension. We would classify this case as vascular-renal if the albumin were persistent; if the urea clearance were less than 50 per cent, or if the ophthalmoscopic findings were marked. Note the subnormal weight gain, rapid increase in blood pressure without other symptoms or signs, little or no edema and absence of albuminuria except at delivery. This patient has a normal renal function and with proper care should live for many years. Repeated pregnancies almost always cause further damage and definitely shorten the life expectancy.

Many articles have been written condemning the radical treatment of eclampsia and praising the conservative treatment. Both terms are poorly chosen. Thus a "conservative" treatment which results in maternal deaths is just as extreme as the radical or accouchement forcé which may also result in a maternal death.

The survey by Eden in 1922 illustrates the difference in mortality between mild and severe eclampsia. Any operative procedure which has a high inherent mortality of its own, necessarily increases the mortality of eclampsia. The mortality for severe eclampsia is definitely lowered by early delivery.

MATERNAL MORTALITY
706 Eclamptic Patients (Eden)

	Mild Per Cent	Severe Per Cent
Natural delivery	5	37
Assisted delivery (forceps)	6	32
Induction of labor	7	26
Cesarean section	11	46
Accouchement forcé	18	63

Hermann reports a close correlation between maternal mortality and the duration of the eclampsia before delivery as measured by the number of fits and by the number of hours before delivery.

MATERNAL MORTALITY
1,633 Eclamptic Patients

Number of Convulsions	Maternal Mortality Per Cent
1–2	7
3–6	14
7–10	21
11–16	28
17–20	37

MATERNAL MORTALITY
1,379 Eclamptic Patients

Number of Hours before Delivery	Maternal Mortality Per Cent
0–2	7
3–4	17
5–8	19
9–12	24
13–21	25
over 21	28

Thus there is a very definite time element in the treatment of eclampsia. Waldstein delivered 117 eclamptic patients within three hours of admission and lost two patients, a mortality of 1.7 per cent. Liepmann reports a mortality of 2.5 per cent and Esch of 1.7 per cent, with early delivery. Hermann reports a maternal mortality of 5.3 per cent in 75 patients brought in to the hospital and delivered as soon as possible and a 12.4 per cent in 250 who had a delayed delivery. He treated nineteen patients in the hospital by early delivery with no deaths and forty-one similar cases by late delivery with a 2.4 per cent mortality.

It is obvious that the lowest maternal mortality is obtained in those patients who deliver relatively soon after the onset of the fits. It is also obvious that the eclamptic patient is not a suitable subject for extensive operative procedures and prolonged anesthesia. We believe that the obstetric treatment is the most logical because it is designed to treat the oliguria or anuria, the cerebral anemia and edema (convulsions and coma) and the arteriolar spasm until the patient can be delivered normally. If the cervix is uneffaced and closed and the case a severe one, delivery should be by cesarean section under local anesthesia when the conditions are ideal for the performance of the cesarean section.

Our treatment is as follows:

General. Constant observation. Retention catheter. The temperature, pulse and respiratory rate, blood pressure and urine volume should be determined every two hours until the patient is conscious. Oxygen is administered for marked cyanosis.

Convulsions. One or preferably more of the following drugs are used: The author uses #1 and #2 antepartum and adds chloral after delivery.

1. Magnesium sulfate 50 per cent solution: 6 c.c. intramuscularly and 2 c.c. after every convulsion until controlled. Maximal amount is 20 c.c. in twenty-four hours.

2. Luminal-sodium: subcutaneously 0.3 Gm. (5 gr.) every eight to twelve hours.

3. Morphine sulfate: 0.016 Gm. (¼ gr.) every hour until convulsions cease or respirations become 12 per minute.

4. Chloral hydrate: 2 Gm. (30 gr.) in 100 c.c. starch water given by rectum every six to twelve hours.

Elimination. Soapsuds enema.

Hypertension. Sedation, especially barbiturates and chloral hydrate.

TABLE III

V. R.—Multipara. 33 years old. 30 weeks gestation. No prenatal care

Day	Treatment	Urine c.c.	B.P.	Temperature	Pulse	Hemoglobin Per Cent
1. 11:00 P.M.	Convulsions 1500 c.c. 20 per cent glucose. Coma	Catheter inserted 0	.....	..	136	127
12:00	.....	940	185/130	39	140	
2. 1:00 A.M.	.....	750	160/128	..	128	
2:00 A.M.	.....	300	136/122			
3:00 A.M.	.....	40	140/100	38	128	
4:00 A.M.	.....	15	130/110	38	120	
5:00 A.M.	Awake	45	128/100	..	120	
6:00 A.M.	1000 c.c. 20 per cent glucose	25	130/110	..	120	
7:00 A.M.	.....	25	.....	..	118	
8:00 A.M.	.....	540	.....	37	106	
9:00 A.M.	Conscious Not clear mentally	300	175/140	..	...	90
Total	2500 c.c. 20 per cent glucose	2980				
11:00 A.M.	Bag inserted	60	150/110	37	128	95
1:30 P.M.	Fetus extracted	75	185/145	37	124	
4:00 P.M.	Nasal tube 50 c.c.	....	180/140	37	112	93
4:30 P.M.	1000 c.c. 20 per cent glucose	300				
5:00 P.M.	Karo 100 c.c.	1000	180/130	37	112	
6:00 P.M.	Karo 150 c.c.	450	.....	37	112	
7:00 P.M.	Karo 200 c.c.	....	.....	37	112	
8:00 P.M.	Karo 200 c.c.	50	.....	37	94	
9:00 P.M.	Karo 200 c.c.	75	.....	37	104	
10:00 P.M.	Karo 200 c.c.	450	.....	37	102	
10:30 P.M.	500 c.c. 20 per cent glucose					
11:00 P.M.	Karo 200 c.c. 6 c.c. 50 per cent $MgSO_4$	600	185/130	37	110	
3. 1:00 A.M.	Karo 200 c.c.	550	.....	37	110	
48 hr. total	4800 c.c. Rational	5500	185/150	37	96	87

Renal and Cerebral Symptoms. The intravenous injection of from 500 to 1000 c.c. of a 20 per cent glucose solution, two or three times daily given within forty to sixty minutes. Sufficient glucose is injected to insure a urinary volume of at least 30 c.c. per hour. A 30 per cent (500–1000 c.c.) or 50 per cent (200–400 c.c.) solution is used if an adequate output of

urine cannot be produced with the 20 per cent or if symptoms and signs of pulmonary edema appear. Normal saline, Ringer's, and bicarbonate solutions are *contraindicated.*

Pregnancy. If the patient is in labor, delivery may be hastened by rupture of the membranes or the use of a bag. If the patient is not in labor, we may, after a diuresis has been established, consider:

A. Induction of labor, as described above or

B. Cesarean section. This operative procedure should only be performed if the case is of the severe type or if cephalopelvic disproportion exists. Local anesthesia should be used and the environment must be suitable.

Diet. Nothing is given by mouth until the patient is conscious. As soon as the stomach is emptying itself, 50 c.c. of a 10 per cent karo syrup solution are injected through a nasal tube and increased 50 c.c. every hour up to the patient's tolerance (usually 200 c.c.) and continued until the patient is conscious and able to take water and fruit juices by mouth.

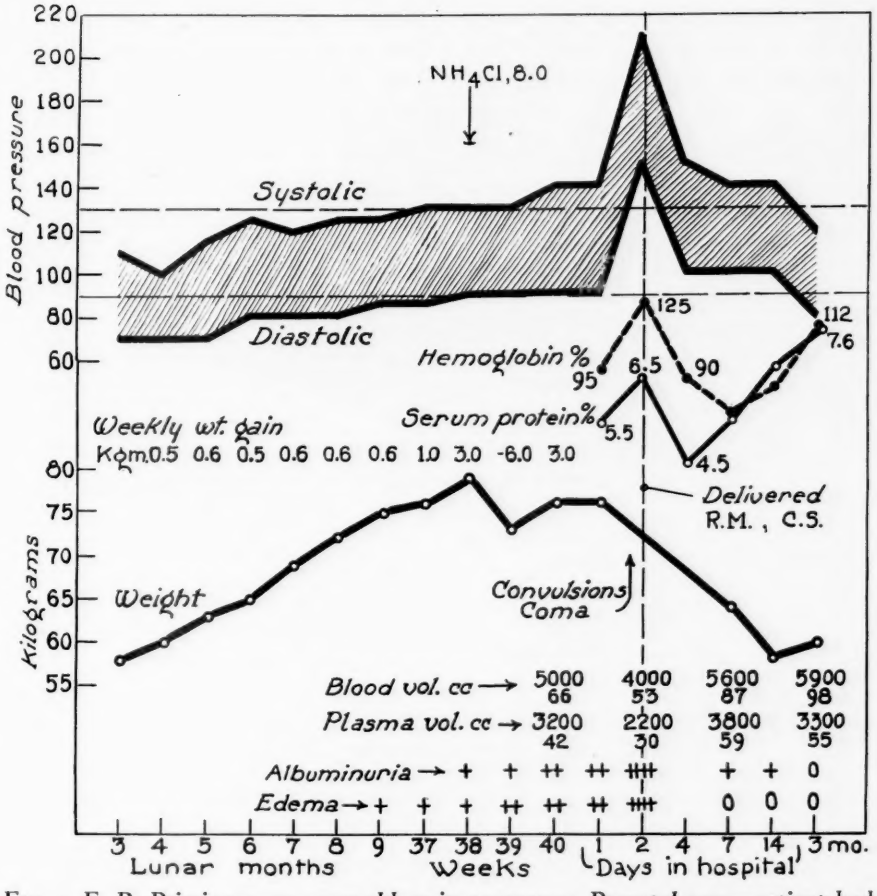

Fig. 1. E. R. Primipara, 20 years old, twin pregnancy. Prenatal care—patient had gained 20 Kg. NH_4Cl was given daily for one week and caused six Kg. loss in weight.

Data for case V. R. given in Table III illustrate the prompt response to treatment. The patient was thirty weeks pregnant and obviously could not be carried to term. Note the marked diuresis, decrease in temperature to normal, decrease in pulse rate and return to consciousness within ten hours after admission.

Figure 1 illustrates the classical case of pre-eclampsia and eclampsia. Excessive

and rapid gain in weight and then the successive appearance of edema, proteinuria, hypertension, and finally convulsions and coma. The patient's course demonstrates that periodic observations are of no value if the abnormal signs are not properly interpreted and treated. The patient should have been sent into the hospital at the thirty-sixth week. The increased hemoglobin from 95 to 125 per cent, and the rise in serum protein from 5.5 to 6.5 Gm. per cent, indicating a blood concentration, are characteristic of eclampsia. The patient three months after delivery had 5900 c.c. of blood and weighed 60 Kg., as compared with a blood volume at term of 5000 c.c. and a weight of 76 Kg. Since the blood volume at term is increased 20 per cent, it should have been 8000 c.c. Note the further decrease in blood volume during the convulsions and coma.

TABLE IV

Day	B. P.	T.	P.	R.	Urine C.c.	Treatment	Wt. Kg.
1. 12 hr...					200	Intake 1,000	76
2. 8 A.M..	150/110	36	76	18		Rupture of membranes	
12.....		36	72	20	25	1,500 c.c. oral	
4 P.M..	175/120	36	66	20	10	Contractions	
8 P.M..	210/150	37	112	24	0	Convulsions 6 c.c. 50 per cent $MgSO_4$ 5 gr. sod. luminal 1000 c.c. 20 per cent glucose	
9 P.M..	170/130	37	110	28	600	Coma	
10 P.M..	165/120				300	6 c.c. $MgSO_4$	
12.....	170/130	38	110	28	140	5 gr. sod. luminal	
3. 2 A.M..	170/130				50	1000 c.c. 20 per cent glucose	
3 A.M..	160/115	39	120	32	150	Coma deeper	
4 A.M..	150/110				75	Convulsions	
5 A.M..	150/95	39	132	36	20	Cesarean section Local anesthesia 1000 c.c. 20 per cent glucose	
7 A.M..	160/115	39	144	32	800	5 gr. sod. luminal	
8 A.M..	160/110	38	132	30	425	30 gr. chloral hydrate by rectum	
24 hr...					2600	Intake 3700	
10 A.M..	155/110				200	Coma	
12.....	160/110	37	120	28	150	1000 c.c. 20 per cent glucose	
2 P.M..	150/105				550	5 gr. sod. luminal	
4 P.M..	155/110	37	110	24	550	Conscious	
8 P.M..	165/115	37	110		750	1000 c.c. 20 per cent glucose	
4. 1 A.M..					1500	1000 c.c. 20 per cent glucose	
8 A.M..	150/100	37	96	22	1800	30 gr. chloral hydrate	
24 Hr..					5500	Rational Intake 5800	
5. 8 A.M..	155/110	37	84	18	4500	Intake 3400	
6. 8 A.M..	140/95				5200	Intake 2900	
7. 8 A.M..	140/100				5500	Intake 3000	64 59
14.	135/75				2900	Intake 3,500	
3 mo.....	120/80					U. C.—110 per cent. U/B 42.	

Table IV covers the same patient as Figure 1 and shows the rapid onset of severe eclampsia. Note the oliguria and ultimate anuria, followed by convulsions. Such a patient should be given sedative drugs and hypertonic glucose intravenously to prevent the onset of convulsions. The response to the first injection of glucose was adequate but despite further sedation and another injection of glucose, the patient had more fits, the pulse and respiratory rates and temperature increased markedly, the urinary output was inadequate and the blood (Fig. 1) became more concentrated. Obviously this is a different case from the preceding one and evidently the patient's condition was critical. The severe case is best treated by early delivery, and as the progress of labor was slow, a cesarean section was performed. After delivery the glucose injection produced a marked diuresis, a blood dilution occurred, and clinical improvement was evident.

These two cases illustrate how the response to a systematic treatment can be used to differentiate between mild and severe eclampsia.

SUMMARY

The gain in weight per week in normal pregnancy should not exceed 300 Gm. A greater gain should suggest too large an intake of food or an abnormality in the water balance, and a gain greater than 600 Gm. should be regarded as being due to retained water. Appropriate treatment should be instituted early.

A systolic blood pressure of 130 to 139 is considered abnormal and a systolic of 140 or more is indicative of pre-eclampsia, essential hypertension, vascular-renal disease, or glomerulonephritis.

Proteinuria in pregnancy is abnormal and should always suggest toxemia. A persistent twenty-four hour excretion of 5 Gm. or more warrants interruption of the pregnancy in the interest of both fetus and mother.

The occurrence of toxemia of pregnancy cannot be prevented, but the proper interpretation and treatment of the above signs will usually prevent the onset of the various cerebral, visual, gastrointestinal, and renal symptoms and signs and thus lessen the possibility of eclampsia.

The obstetric treatment of eclampsia yields the lowest mortality. It comprises the control of the convulsions, the promotion of an adequate urinary output, and the securing of a normal temperature, pulse and respiratory rate, a conscious patient, and an early delivery.

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A NEW CLASSIFICATION OF THE TOXEMIAS OF PREGNANCY*

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ADVANCE in our knowledge of the toxemias of pregnancy has undoubtedly been impeded by the lack of a uniform classification of these disorders. Our ignorance as to etiology and the similarity of features of certain of these conditions are among the main reasons for confusion in regard to definition and classification of the toxemias, as is apparent in the literature and published hospital reports. Individual attempts at clarification of the problem and evolution of a standard, workable classification, which all interested would be willing to use, have thus far failed. Some years ago Kellogg wrote: "The conquest of the toxemias of pregnancy depends primarily on a universal acceptance in this country of some index, of some classification, some coöperative mode of study in every great obstetric center."

Realizing the desirability of a uniform classification, the American Committee on Maternal Health, in 1937, appointed a committee consisting of Drs. R. D. Mussey, E. T. Bell, F. S. Kellogg, W. W. Herrick and H. J. Stander to study the problem and, if possible, to reach an agreement upon a simple, workable classification. As the etiology of certain of the toxemias is as yet unsolved and differences of view still exist, it is inevitable that, to accomplish the above-stated purpose, the various members of this committee must be willing to compromise with regard to individual concepts. The fact that the committee has been able to arrive at a mutually satisfactory, tentative classification is indeed gratifying, and it is hoped that maternity hospitals throughout the country will be willing to adopt the final grouping of the Committee. The Chairman of the Committee, Dr. Mussey, has given the author permission to publish the new classification thus far evolved and agreed upon by all members.

It will serve no useful purpose to discuss here previous classifications, except to indicate how they may be correlated with the following new classification proposed by the Committee:

1. Hypertensive disease
2. Renal disease
3. Pre-eclampsia, severe
   Pre-eclampsia, mild
4. Eclampsia
5. Vomiting of pregnancy
6. Acute yellow atrophy of the liver
7. Unclassified

On April 1, 1939, the above classification was adopted in the New York Lying-in Hospital, and in Table 1 are given the relative incidences of the various types. It will be seen that mild pre-eclampsia accounts for almost 50 per cent of all toxemias. Under this group are included most of the cases which were formerly indexed as "low reserve kidney." The second most frequent type is hypertensive disease, which includes a large percentage of our cases hitherto grouped as "unclassified," as well as some of the low reserve kidney cases. The other types—vomiting, acute yellow atrophy of the liver, eclampsia, severe pre-eclampsia and renal disease, are identical with the earlier classification used in our clinic, except that the term "chronic nephritis" has been replaced by "renal disease." The relative incidence of

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these types thus remains as in our previous studies of the toxemias.

The specific types which need no discussion in this paper since they are similar to, and to a large extent synonymous with, the majority of previously published classifications by various authors, are: vomiting of pregnancy; acute yellow atrophy of the liver; eclampsia; pre-eclampsia, severe; renal disease. For purposes of clarification, however, it should be stated that "pre-eclampsia, severe" includes those cases which in most classifications have been termed "pre-eclampsia," and that "renal disease" is an inclusive term comprising all cases of kidney disease or chronic nephritis of whatever type—chronic glomerulonephritis; arteriosclerotic nephritis (nephrosclerosis); or nephrosis (degenerative type of nephritis). Under "renal disease" should be indexed all patients in whom the past history, present symptomatology and signs, laboratory and chemical findings, such as kidney function, blood chemistry and eye-ground changes, indicate involvement of the kidneys. In "borderline" cases extended observation and clinical and laboratory study may be necessary before a definite diagnosis of kidney involvement or "renal disease" can be established. This, however, is not different from the procedure essential to making the diagnosis of "chronic nephritis" of earlier classifications.

The new terms or designations in the Committee's classification which need some explanation are: pre-eclampsia, mild; and hypertensive disease.

Mild Pre-Eclampsia. By mild pre-eclampsia we indicate those patients suffering from a slight rise of blood pressure, some albuminuria and perhaps edema during the latter part of pregnancy; in other words, the findings of pre-eclampsia, but to a limited extent. Shortly after delivery these abnormalities completely disappear and may not reappear in a subsequent pregnancy. In the past this condition has been variously designated. In 1926, Stander and Peckham called this type "low reserve kidney"; it has been labeled "non-convulsive toxemia," "hypertensive toxemia," "hypertension of pregnancy," "albuminuria of pregnancy," "recurrent toxemia," and "kidney of pregnancy." In 1937, Kellogg suggested the term "mild pre-eclampsia."

The following description of this group, taken from Stander and Peckham's paper of 1926, will serve to identify the condition:

"1. An elevated blood pressure which at the end of the puerperium has dropped to a normal level. In most instances this elevation is not very marked, being approximately 150 systolic and 90 diastolic.

"2. The amount of albumin in the urine is never very great, varying before delivery between a fraction of a Gram and 2 Gm. per liter, although the lower figures are most usually observed. The albumin disappears during the puerperium, and the patient leaves the service either with no albumin at all, or with at the most 0.1 Gm. per liter.

"3. The outstanding characteristic is the fact that in subsequent pregnancies, the patient's condition does not become aggravated, and she is as well as, or better than, in the preceding pregnancy.

"4. The blood chemistry, as well as the urine chemistry, reveals nothing abnormal."

Hypertensive Disease. Hypertensive disease (hypertensive vascular disease; diffuse arteriolar disease with hypertension; essential and malignant hypertension), just as renal disease, is not a toxemia of pregnancy, but is included in the classification because it is so often first recognized during a pregnancy, is apparently accentuated by gestation, and simulates, in certain features, pre-eclampsia as well as renal disease. Thus it is essential to both proper evaluation and correct diagnosis of the true toxemias of pregnancy, that we include and discuss hypertensive disease, or what has been termed by Keith and his associates, "diffuse arteriolar disease with hypertension."

The syndrome "essential hypertension" has been recognized for many years, and as

the name implies, signifies an elevated blood pressure based upon no apparent associated pathology. Since 1914, when Volhard and Fahr recognized two distinct forms, benign and malignant, essential hypertension has received intensive study both as to its cause and final outcome. The work of Keith, Mussey and their group, Goldblatt and his associates, Pickering, Allen and Adson, Page and Heuer, Nowak and Walker, and of many other investigators, has brought us to a clearer understanding of this condition. In 1932, Goldblatt produced hypertension by constriction of the renal arteries with silver clamps. The subsequent work of the past eight years indicates that this experimentally produced hypertension results from renal ischemia and may be dependent upon humoral influences such as may come from the adrenal cortex and perhaps the kidney itself. Normal blood pressure is maintained by the force of the cardiac contractions, the tonus of the vascular system, the volume and viscosity of the blood and the peripheral resistance. In essential hypertension in man, the cardiac output as well as the volume and physical state of the blood are normal, whereas it is generally agreed that peripheral resistance is increased due to involvement of the arteriolar walls. There is divergence of opinion as to whether human hypertension is of similar origin as experimental hypertension, although some evidence suggests that it also is dependent upon renal ischemia. The peripheral resistance in essential hypertension may be caused by morphologic changes in the arterial vessels, or vasoconstriction of chemical or nervous origin. Experimental evidence has apparently ruled out vasoconstriction of nervous origin. It may well be, as above indicated, that morphologic changes as well as chemical factors play a rôle in the production of essential hypertension. There is little doubt that experimental hypertension, such as that produced by the Goldblatt clamp, is chemical in origin.

In our clinic, Dill and his associates have been investigating experimental hypertension in the pregnant animal and have definitely shown that a clinical syndrome characterized by hypertension, albuminuria, and hematuria, and by pathologic findings of necroses in the kidneys, liver, myocardium and placenta results from renal ischemia produced during the pregnancy, although no obvious effect seems to accompany or result from pregnancy in an animal previously rendered hypertensive.

Hypertensive disease may antedate pregnancy or may first appear during gestation. It is conceivable that pregnancy is a predisposing factor in the production of arteriolar changes resulting in hypertension, which may become permanent in the form of an "essential hypertension." Certainly pregnancy is accompanied by vascular changes, such as spasm of the arterioles, which may conceivably play a rôle in the production of hypertension.

The characteristic finding in this condition is an elevated blood pressure without any signs or symptoms indicative of renal involvement. The past history, the first appearance and course of the hypertension, the evaluation of other signs or symptoms, the laboratory findings as they relate to kidney function and the examination of the eyegrounds are the main factors in establishing a correct diagnosis. It is essential to rule out renal disease, after which it becomes necessary to determine the extent of the arterial disease. To this end, examination of the eyegrounds is all important.

In the benign form of hypertensive disease, the blood pressure is usually not elevated to extreme degrees, no albuminuria exists, ophthalmologic examination reveals only minimal changes in the vessels and symptoms are commonly absent. In the severe forms, or malignant type, the retinal vessels show more marked involvement, and finally kidney function becomes impaired. It is thus clear that from the benign form, there is a transition to the malignant type where the condition sooner or later shows renal involvement.

Keith and his group have divided hypertensive disease or what they prefer to call "diffuse arteriolar disease with hypertension," into four groups, the first being the well recognized benign essential hypertension; the second including those with more marked hypertension, slight symptomatology and no retinitis; the third, those with mild vasospastic retinitis; and the fourth, the malignant hypertension. The retinal changes proceed from minimal involvement to angiospastic retinitis, to edema of the discs with spastic and organic narrowing of the arterioles with diffuse retinitis.

DISCUSSION

It is not the purpose of this paper to discuss prognosis and treatment in the various groups or types of toxemia, but merely to outline the new classification. That this classification is simple and workable is shown by the fact that we have employed it during the past nine months without undue difficulty in the transfer from our previous to the present classification. To a certain extent we have been able to correlate the statistics of the previous seven years with this new classification, as is shown in the accompanying tables, and particularly in that representing our maternal mortality figures for the whole period.

Table I
INCIDENCE OF TOXEMIA—NEW CLASSIFICATION
108 Cases in 1,503 Pregnancies
(April 1, 1939—September 30, 1939)

Type of Toxemia	No. of Cases	Percentage of Total
Vomiting of pregnancy	7	6.5
Acute yellow atrophy of liver	1	0.9
Eclampsia	4	3.7
Severe pre-eclampsia	7	6.5
Mild pre-eclampsia	51	47.2
Hypertensive disease	31	28.7
Renal disease	7	6.5
Total	108	100.0

From Table I it will be noted that the total incidence of toxemias, including renal and hypertensive disease, is slightly over 7 per cent. Mild pre-eclampsia and hypertensive disease together account for about three-fourths of the whole series. Renal disease, severe pre-eclampsia and vomiting of pregnancy are of equal frequency and of about the incidence reported in our earlier studies, where these types were designated as chronic nephritis, pre-eclampsia and vomiting of pregnancy, respectively. We have had an unusually high incidence of acute yellow atrophy of the liver, as shown in Tables I and III. In Table II are recorded the maternal mortality rates in the 2,276 cases of toxemia, treated in the New York Lying-in Hospital during the period September 1, 1932 to December 31, 1939, while in Table III are given all maternal deaths occurring in our service during the same period. From these tables it will be noted that the toxemias of pregnancy accounted for 7.1 per cent of our total uncorrected maternal mortality in 30,457 patients dis-

Table II
MATERNAL MORTALITY IN THE TOXEMIAS OF PREGNANCY

Type of Toxemia	Maternal Deaths	
	No. of Cases	Percentage Incidence in 2,276 Toxemias
Vomiting	0	0
Pre-eclampsia, mild (low reserve kidney)	0	0
Pre-eclampsia, severe	0	0
Eclampsia	1	0.044
Renal disease (chronic nephritis)	0	0
Hypertensive disease (unclassified)	0	0
Acute yellow atrophy	3	0.132
Total	4	0.176

Total toxemia mortality:
4 maternal deaths in 2,276 pregnancies, or 1.76 per 1000 pregnancies

charged from the hospital. The toxemic deaths occurred in acute yellow atrophy of the liver and in eclampsia. During the seven year period we had eight cases of acute yellow atrophy with three deaths, or a mortality of 37.5 per cent; while during the same period we had forty-seven cases of eclampsia with one maternal death, or a mortality rate of 2.1 per cent. It may be of interest to state that the fatal cases of acute yellow atrophy of the liver showed the typical clinical picture as well as the pathologic lesions in the liver at autopsy.

SUMMARY

The number of cases of toxemia of pregnancy recorded in this paper is too small to allow definite conclusions. However, the analysis of this series indicates that the new classification of the Committee appointed by the American Committee on Maternal Welfare, can readily be applied, being simple and workable. Although the author has been an advocate of certain different concepts, he is more than willing to use this classification in the indexing and study of the material in the

TABLE III

MATERNAL MORTALITY FOR PERIOD

September 1, 1932—December 31, 1939

Pavilion, Private and Berwind (Outdoor) Services

During this period there were 56 deaths in 30,457 discharged patients, a maternal mortality rate of 0.184 per cent, or 1.84 per 1000 patients discharged, or 2.06 per 1000 pregnancies. The causes of death in these fifty-six patients are shown in the table.

Cause of Death	1932	1933	1934	1935	1936	1937	1938	1939	Total	Per Cent of Total
Infections:										
Antepartum and postpartum	..	1	1	3	4	1	..	1		
Postabortal	..	..	..	..	1	..	1	..	13	23.2
Pneumonia:										
Antepartum and postpartum	2	1	..	2	..	1	..	..	6	10.7
Postpartum hemorrhage:										
Vaginal delivery	1	..	..	1	..	1	1			
Following section	..	..	1							
Ruptured uterus	..	1	..	..	..	..	..	..	6	10.7
Cardiac disease:										
Cardiac failure	..	1	..	1	1	..	1			
Postpartum hemorrhage	..	..	..	..	..	1	..	..	5	8.9
Pulmonary embolus	1	..	2	1	..	..	1	..	5	8.9
Toxemia:										
Acute yellow atrophy	..	1	..	..	1	..	..	1		
Eclampsia	..	..	..	..	..	1	..	..	4	7.1
Premature separation of placenta	..	..	1	..	1	1	..	..	3	5.3
Pyelonephritis	..	1	..	1	..	..	..	..	2	3.6
Circulatory collapse:										
Pituitrin intravenously	..	..	..	1						
Surgical shock	..	..	..	..	..	1	..	..	2	3.6
Cerebrovascular accident	..	..	..	1	1	..	..	..	2	3.6
Anesthesia	..	1	..	..	..	..	..	..	1	1.8
Postoperative hemorrhage	..	..	1	..	..	..	..	..	1	1.8
Tuberculosis, miliary	..	..	..	1	..	..	..	..	1	1.8
Placenta previa, antepartum	..	..	..	1	..	..	..	..	1	1.8
Chorionepithelioma (postpartum)	..	..	..	..	1	..	..	..	1	1.8
Blood dyscrasia-erythroblastic splenomegaly	..	..	..	..	1	..	..	..	1	1.8
Suicide	..	..	..	1	..	..	..	..	1	1.8
Not determined—insufficient data	..	..	..	..	..	1	..	..	1	1.8
Total	4	7	6	14	11	8	4	2	56	100.0

New York Lying-in Hospital, and hopes that all maternity services throughout the country will adopt this new classification. Should this obtain, we would be in a far better position to gain valuable information regarding the etiology and treatment of these disorders of pregnancy. Cooperative studies, similar to those already being conducted by the cooperative clinical group interested in syphilis complicating pregnancy, are most desirable, but, of course, cannot be successfully carried out unless all clinics entering into such a study employ a uniform classification.

Mortality among the offspring of toxemic mothers is appreciably higher than among those without toxemia. . . . A large proportion of the deaths is probably due to procedures instituted because of the toxemia rather than to the disease itself.

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

NUTRITION IN PREGNANCY

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OF prime importance in maternity care is the nutrition of the expectant mother. She must be regarded in a class apart, with many special needs to be considered. In these days of altered economic conditions there is an added difficulty of adjusting the family food budget to provide the adequate and essential food items for the pregnant and nursing mothers. The deficiencies of the diet of the non-pregnant woman become dangerous when maternity intervenes. It has been shown by many surveys that the diets of adults show deficiencies in various items ranging from 40 to 90 per cent, and in prenatal groups the deficiencies in essential items may range from 12 to 50 per cent.

Nutrition requirements are usually stated under four headings: a minimum or maintenance level; a level adequate for health, a 50 per cent increase over the minimum; an optimum nutrition level; and curative levels. In pregnancy we should at least hope for an "adequate for health" level. Such a diet should provide protective, energy giving and regulatory constituents. It should have the ingredients so balanced that no drain is placed on body tissue; it should provide for growth of the woman's body as pregnancy advances; and while supplying the fetus with material for growth, still be sufficient to put aside a reserve for the work of labor and for the onset of lactation.

What should a proper diet for a pregnant woman contain and how may we educate and help her to obtain it? It is not enough to advise her to drink plenty of water, eat vegetables and go lightly on starches and meat. Such advice is worse than none. It is necessary to be specific and yet use terms which are understandable by the average citizen. That 1 Gm. of calcium per day is essential, is Greek to a clinic patient, but that she should drink a quart of milk a day is common sign language. Yet, if we do not understand the Greek ourselves we cannot translate our knowledge into the sign language of milk, meat, grains, and greens.

The average weight gain during pregnancy amounts from 20 to 25 pounds. Dieckmann[1] recommends limiting the weight gain to the equivalent weight of the fetus, placenta, amniotic fluid, and the maternal physiologic changes incidental to pregnancy. In other words about 16½ pounds (7.5 Kg.) or an average weekly gain of ½ pound after the end of the negative phase of pregnancy.

A controversial point in regard to weight gain during pregnancy and the birth weight of the child still exists. Rucker[2] feels that a carefully calculated diet, low in fluid, fat and carbohydrate, high in protein, and with a total of 1800 calories has definitely reduced the weight of babies, shortened the length of labor and caused a minimum of premature babies compared with a control group. Unless such a diet provides the essential food constituents it may do harm, and the parasitic action of the fetus will be at the expense of the maternal organism.

The energy requirements or heat units or calories of a pregnant woman's diet vary with her weight and with her activities. If we accept as a standard 30 calories for every 2.2 pounds, we should add 75 calories for each hour of active moderate work. Thus, the average woman (120 to 150 pounds) would need from 2000 to 2500 calories, while the nursing mother would need a decided increase, from 20 to 40 per cent. Calories, or heat units, are derived from three principal ingredients of the diet:

protein, fat and carbohydrates. These are the building and energy giving sources of our diet.

Protein is required in proportion of 1 Gm. or 15 gr. for every Kg., or 2.2 pounds of body weight. Proteins are derived from two sources: animal and vegetable. The proteins break down in the body to form elemental units, called amino acids. These units serve to build and repair the body tissues, promote growth of the fetus and to keep the nitrogen balance level. The animal proteins, derived from animal tissues, meat, milk, eggs, cheese, form or should form, half of protein requirements. The remainder will come from the vegetables: peas, beans, and other sources. A high protein diet in the expectant mother is believed to raise the prothrombin and fibrinogin content of the maternal blood, and so protect against hemorrhage.

Certain proteins such as lactalbumin of milk, beef protein, ovalbumin of eggs and glutinin of wheat, contain all the essential amino acids and the average diet should contain all these articles to prevent a qualitative deficiency. The reserve or deposit protein in the adult human body amounts to approximately 2 Kg. or 5 pounds. During the latter five months of pregnancy approximately 500 Gm. of nitrogen is stored up as a reserve for labor and lactation. The protein requirement for the fetus has been given as 60 Gm. of nitrogen, for the placenta 17 Gm., the amniotic fluid 1 Gm., the mammary glands 17 Gm. and for the uterine enlargement as 39 Gm.

From a table of food values it is simple to ascertain the approximate protein sufficiency of a diet. Thus one serving each of milk, eggs and roast beef with three servings of bread would contain 1100 calories and yield 54 Gm. of protein, four-fifths of the protein requirements of the average woman. Over 70 per cent of this is protein of high biological value.[3]

Vegetable proteins are animal protein savers, but they are inadequate sources of amino acids and should only be used as an accessory source of protein supply. McCarrison[4] feels that 66 per cent animal protein in the diet, recommended by the Nutrition Committee of the League of Nations,[5] is an unnecessarily high figure. He recalls the high biological value of the vegetable group of proteins. Many unemployed and low paid families are unable to purchase even a minimal animal protein maintenance ration.

Deficiency in protein in pregnancy may lead to nutritional edema and tend to anemia, poor muscular tone, lowered resistance to disease, and poor milk supply. Restriction of protein lowers the nitrogen level and leads to nutritional edema due to utilization of the body tissues for the normal protein requirements.

The two groups of energy supplying foods are carbohydrates and fats. Fat is not only a concentrated source of energy, but is of primary importance as a carrier of essential vitamins, and may be essential to their proper utilization. From observation of women who choose their own diets, it seems that fat intake is fairly steady throughout pregnancy. The observed intakes vary from 103 to 139 Gm., and these values are well above those suggested by the Royal Society Food (War) Committee[6] of 100 Gm. per man. Deficiencies in fats may lead to diminished fertility. Excessive fat ingestion has been suggested as a cause of eclampsia. Butter may be regarded as the best fat.

The number of calories or heat energy units required in a diet, after the adequate requirements of protein have been met, are made up in part of fat which represents 25 to 30 per cent. The remaining calories are derived from carbohydrates, 50 to 60 per cent, which are essential in the diet only as a source of energy, supply for food for the growing fetus, and to spare the proteins from being burnt up by the higher metabolic rate of pregnancy. Their intake must be carefully controlled, for an excess of carbohydrates leads to a diminished intake of proteins and vitamins. Excesses in

carbohydrates lead to an unhealthy gain in weight.

One of the most frequent forms of carbohydrate used in excess in the diet of pregnant women is white bread, which is cheap and bulky. There has been insufficient insistance on the total substitution of whole grain bread for white bread. The highly milled flours and cereals are deprived in the milling of important nutritive elements, such as the vitamin B complex, vitamin E, unidentified blood making factors and the proteins of the germ and bran. A slice of whole wheat bread not only has the same caloric value as a slice of white flour bread but it possesses a greater value in calcium, phosphorus, iron and vitamin B. Carbohydrates in the diet may easily be lowered by shifting to 5 per cent or 10 per cent vegetables from those with a higher carbohydrate content.

Various mineral constituents of the diet are essential for the nutrition of the expectant mother. We may discuss the three most important: calcium, phosphorus and iron.

Calcium. The estimated intake of calcium should approximate 1 Gm. per day in the first four months of pregnancy and then be stepped up to 1.5 Gm. in the last five months. This increase is due to the observation that a pregnant woman begins to store calcium and build up a reserve after the fourth month, at which time the fetal demands begin; the fetus begins a storage of its own after the seventh month. A full term fetus contains an average of 24 Gm. of calcium.

The basic source of calcium in the diet of a pregnant woman should consist in a daily quart of milk, which contains 1.15 Gm. of calcium. Skim milk contains just as much calcium as whole milk and may be used if the fat of the cream is not desired in the caloric requirements. The remaining calcium needs should be supplied in other dairy products. If milk is not palatable, an attempt may be made to supply the whole requirement by commercial preparations of calcium. The difference in cost is apparent.

Every organ in the body is influenced by or has an influence upon the calcium metabolism. The utilization of calcium in the body depends upon a proper supply of sunshine or vitamin D. Even with a very high calcium and phosphorus intake, these minerals will not be utilized without an adequate dosage of vitamin D.

A deficiency in the calcium intake leads to many abnormal states. The mother suffers from cramps in the legs, headaches, insomnia. A deficiency may be the cause of dental caries. Eclampsia has also been alleged to be due to a deficiency of calcium. In the fetus of the first pregnancy of a mother whose diet is deficient in calcium, no signs of the deficiency are noted, for the fetus is parasitic, and will drain its necessary lime salts from the host. In rapidly succeeding calcium deficiency pregnancies, however, the fetus is said to suffer from osteoporosis, rickets, and poor tooth formation.

Phosphorus is widely distributed in an average diet containing milk, eggs, meat, fish, cheese, and poultry, and generally little lack is seen. Its mobilization again depends upon vitamin D, and a proper ratio, 1 to 1.5, must be maintained with calcium in the blood.

Iron. It has been calculated that a pregnant woman requires 20 mg. of iron daily. A total storage of 900 mg. of iron is required during pregnancy, for the human fetus at term contains 400 mg., while 500 mg. of iron is required for the placenta. Women in the reproductive cycle, subject to the recurring blood loss of the menstrual flow have high iron requirements. The need of iron is increased in both pregnancy and the nursing period. The increased fluid content of the blood in pregnancy leads to a diminution of the hemoglobin which has been termed, "the physiologic anemia of pregnancy." In many instances secondary anemia is present, and, rarely, a pernicious type is found. It is common to find hemoglobin reading in pregnancy below 70 per cent. Many women need an iron intake greater than can be attained in their diets,

and commercial preparations should be administered, especially in the last trimester of the pregnancy.

Iron is found in beef, liver, egg yolk, oysters, some pitted fruits and in leafy vegetables. It is surprising to note that one-half cup of cooked mustard greens contain as much iron as a generous serving of corned beef or six oysters, and one serving of liver a week will greatly supplement the iron content of other foods. The addition of wheat germ to the diet adds a considerable amount of iron as well as increasing the storage of available iron from other sources. This is but another argument for the use of coarsely ground wheat cereals and flours. The deficient diets of the poorer classes often show clearly in the anemic, pasty-faced, weary and dreary looking pregnant women of our clinics, the lack of available iron supply.

Iodine. A deficiency of iodine affects both reproduction and lactation. For this reason fish or sea foods should be ordered at least once a week in the diet of a pregnant woman. In goiter belts iodized salt should be used in the diet as a prophylactic against disorders of the thyroid gland.

Salt (Sodium Chloride). Both the sodium and the chlorine ion in table salt when used in excess have been blamed as causes of toxemia of pregnancy. Excessive use of salt leads to a retention of water in the tissues. Consequently, a reduction in salt intake and the sodium ion toward the end of pregnancy or where kidney insufficiency is suspected, is in order.

Water. This regulative factor of the diet is generally required in the proportion of 1 Gm. or c.c. for each caloric value of food intake. Intake of 2 liters (2 quarts or eight glasses, large size) would be required to supplement the average diet. The fluid content of various foods lowers the amount of water to be drunk.

Generally speaking the amount of water required is that sufficient to promote a proper dilution of minerals in the blood. An output of 3 pints of urine daily is objective evidence of an ample fluid intake. When edema arises in pregnancy, nephritis must be looked for, nutritional edema ruled out and a water balance must be established, intake being measured to approximate the output, changing the amount daily as required. That 10 pounds of fluid may accumulate in the body tissues before clinical edema becomes evident is of importance in a consideration of weight changes during pregnancy (Bierlein).

"Most estimates of requirement for vitamins today are based on determinations of the minimum amount necessary to prevent visible and recognized symptoms of deficiency, plus a factor of safety to cover individual variations. The size of the factor of safety varies with the viewpoint of the estimator. Such estimates when applied in dietary surveys supply a means for detecting gross deficiency but they do not tell adequacy, if we mean by the latter term amounts necessary to provide optimum needs, optimum health." Strauss[7] states: "I feel that it is wise to hold out for high levels, particularly in view of the many metabolic and gastrointestinal changes which occur in pregnancy and which probably alter the absorption, utilization and requirement of nutritional factors."

There is increasing evidence that mild and frequently unrecognized deficiencies of some vitamins are prevalent in this country. They are due to such factors as inadequate diet (economic), unbalanced diets (ignorance or idiosyncrasies); loss of vitamins (cooking) and ignorance regarding extra requirements.

Vitamin A is fat soluble. It is found in halibut and cod liver oil, butter, milk, cream, and egg yolk, green and pigmented vegetables. The daily requirement in the diet of a pregnant woman has been variously calculated as from 5000 to 9000 International Units. Presence of this vitamin promotes growth and has been said to prevent infection and has much to do with promoting the reproductive process. Qualitative dark adaptation time tests readily show deficiencies. Some skin conditions of pregnancy have been found amenable to

increased intakes of vitamin A and calcium. Since this vitamin is soluble in mineral oil, it has been recommended to avoid such laxatives at meal times.

Vitamin B_1 is soluble in water and is easily destroyed in cooking as it is susceptible to heat. It is found in whole grain cereal, brewer's yeast, meat and vegetables. It is essential in pregnancy since it aids digestion, stimulates the appetite, has a protective function for the nervous system and stimulates lactation.

Minor degrees of B_1 deficiency are seen in the marked nausea and vomiting cases of early pregnancy. Extreme deficiencies are reflected in the polyneuritis and paralysis present in pernicious vomiting cases. Lack of a certain fraction of the B_2 group of vitamin leads in tropical countries to a pernicious type of anemia. In India one-third of maternal deaths are due to this disease. Daily requirements of vitamin B_1 are estimated at 300 to 1200 International Units. Expressed in terms of thiamin chloride, 1 to 1.4 mg.

Vitamin C is found in raw vegetables and the citrus fruits. It is essential for its effect upon the dental apparatus and bones. Its ingestion is said to promote good tooth and bone formation, to prevent bone lesions, to prevent scurvy, and is concerned with the cellular nutrition of the pulp peridental membranes. Indeed, modern dental nutritional studies suggest that vitamin C from the standpoint of the mother, is of almost as great importance as calcium. The sore gums or acid mouth of many pregnant women is a manifestation of a deficiency of this vitamin, and immediate relief is seen when four to six whole oranges are eaten each day. The old saying, "a tooth for a child" is probably due as much to a lack of vitamin C as to a lack of calcium in the diet. It has been recommended that in the daily diet of pregnancy 1500 International Units of this vitamin or 75 of ascorbic acid be included. This is roughly equivalent to the ascorbic acid (or vitamin C) content of three medium sized oranges.

The ascorbic acid intake is closely reflected in the blood serum content of this dietary factor. The fetus draws like a parasite on the vitamin C supply of the maternal host, the umbilical cord blood containing from two to four times the amount of ascorbic acid present in the maternal blood.[8] This suggests that an oversupply is required by the nursing mother, particularly one who has a premature baby. A deficiency in the vitamin C content of the maternal diet is also said to lead to a latent scurvy in the fetus, and to a predisposition to brain hemorrhages in labor.

Vitamin D is essential for proper utilization of calcium and phosphorus. Like vitamin A, it is fat soluble, and is found in fish liver oils, milk, and egg yolk. In addition to mobilizing calcium and phosphorus, it aids in preventing fetal rickets. It is possible that grave deficiencies leading to calcium metabolism disturbances may lead to the production of postpartum hemorrhage. A deficiency may tend to occasion prematurity of labor. It is the current impression that this vitamin should be administered to all pregnant women, summer or winter. It is interesting to note that far larger amounts of vitamin D are used in animal husbandry for cattle, swine, and poultry than are employed for human consumption. As yet, no basic requirements of vitamin D for the pregnant woman have been worked out, and recommendations vary from 300 to 800 units.

Vitamin G is one of the subdivisions of the vitamin B complex group. If B_1 is supplied in sufficient amounts little worry need be had over the other fractions in the diet. Nicotinic acid and riboflavin may be prescribed for appropriate clinical deficiencies.

Vitamin E, the fertility vitamin, is present in such sources as wheat germ oil and lettuce. It may be added to the diet in abnormal cases, as habitual abortion or repeated premature labors, or in the occasional patient, pregnant after a long sterile period, where it appears necessary to

supplement the natural reproductive forces and functions.

SUMMARY AND CONCLUSIONS

The nutritional factors in pregnancy vary with the weight and activity of the particular individual, and must be increased as pregnancy advances.[9] For an average woman of 125 to 150 pounds, active in her domestic life, from 2000 to 3000 calories may be indicated. This value should be derived from a diet containing from 60 to 100 Gm. of protein, 70 to 100 Gm. of fat, 150 to 400 Gm. of carbohydrates. The mineral requirements should range from 0.7 to 1.5 Gm. of calcium, 1.0 to 1.5 Gm. of phosphorus, 20 mg. of iron. The vitamin requirements are: from 4000 to 8000 International Units of vitamin B, or, expressed as thiamin chloride, 0.3 to 1 mg.; from 400 to 2000 International Units of vitamin C, or, expressed as ascorbic acid, 20 to 100 mg.; and 300 to 800 U.S.P. units of vitamin D.

Murphy and Bowes[10] have suggested as basic foods for the diet during pregnancy the use daily of:

1 quart milk
2 to 3 servings of leafy vegetables
2 to 3 servings of other vegetables
3 to 4 servings of fruit (1 or 2 servings of citrus fruit)
3 or more slices of bread, whole grain varieties preferred
Meat or fish as recommended by physician
1 egg
1 to 2 ounces of butter
Cod liver oil or vitamin A, B, D and concentrates, as directed by physician.

The following sample day's diet issued by the Children's Bureau of the United States Department of Labor furnishes a working basis on which modifications may be planned.

Breakfast

Orange
Oatmeal with whole milk
Toast and butter
One cup of coffee, tea, or a glass of whole milk

Dinner

Pot roast of beef or other lean meat
String beans or carrots or both
Baked potato, bread and butter
Glass of whole milk
Baked custard

Supper or Luncheon

Baked rice and cheese
Apple and celery salad
Whole wheat muffins and butter
Stewed apricots
One cup of cocoa made with whole milk, or a glass of whole milk
A glass of whole milk may be taken before bedtime.

An analysis of this diet shows that it contains the following values:

Protein	Fat	Carbohydrate	Calories	Calcium	Phosphorus	Iron	Vitamins in Sherman Units					Excess	
							A	B	C	D	G	Acid	Base
65.35 Gm.	70.55 Gm.	250.25 Gm.	1966	1.446 Gm.	1.695 Gm.	14.10 mg.	9803	401	129	24	427	28.6	49.0

It will be noted that this diet approximates the average optimal requirements for pregnancy.

While the iron value is slightly below the average stated requirements it could easily be made up by an additional beef or calf liver ration twice a week. The deficiency in vitamin D is indicative of the need for its supplementary administration in the diets of many women, particularly in the northern part of the United States in the cloudier seasons of the year.

SUMMARY

In summary it may be said that not until recently has the nutritional aspect of maternity care received the attention it deserves. Only two standard textbooks carry anything but a cursory mention of the subject.[11,12]

The possible relation of dietary factors to such problems of pregnancy as toxemia and prematurity are beginning to be recognized and investigated.

The health and well being of the pregnant woman and her unborn fetus demand an enlarging interest in the question of nutrition.

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It must constantly be remembered that merely because a woman suffering from toxemia gives birth to a dead fetus, this is no proof that such condition was responsible for its death, and other causes should be sought as diligently as if toxemia were absent.
From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

NATURAL LABOR

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NATURAL labor is the ideal objective for the termination of every pregnancy. In order to accomplish this it is absolutely necessary that the patient have the benefit of intelligent obstetric management, not only during labor, but throughout the duration of the pregnancy and the puerperium. A very large proportion of all labors will proceed to a natural termination, if permitted. Errors of commission are much more common in obstetric practice than errors of omission. The recognition at the earliest possible time of abnormal conditions may do much to secure a normal labor or minimize the dangers that are to be anticipated.

In reviewing protocols of fatal obstetric results several facts are outstanding. First, a labor which would have been natural has been converted into an unnatural labor by unwise and unnecessary interference on the part of the attendant; second, failure to recognize abnormal conditions early enough to anticipate bad results and conduct the case in such a manner that the best results could be secured under the conditions present, or in some instances to change an abnormal labor into a natural labor; third, unwise selection of the procedure best suited to the pathologic conditions present; fourth, although the proper operative procedure may have been chosen, it is done at the wrong time.

The practice of obstetrics is coming quite definitely under the influence of this fast age and the old dictum that "to do good one must do no harm" seems to have been forgotten. The attendant has no moral right to do anything which will even to the slighest degree increase the hazard to his patient. It is a fact that any interference, however simple, during the progress of labor is potentially harmful and the reasons for doing anything must greatly outweigh the disadvantages of doing nothing. The experienced obstetrician too frequently finds himself confronted with the necessity of steering between Scylla and Charybdis with danger to the mother on one hand and to the baby on the other. Many procedures have been proposed to accomplish some doubtful purpose, which in themselves definitely increase the dangers to the mother and the baby. The purpose of the doctor should be to keep out of trouble; all too often the death of the baby or the mother is directly due to overactive interference with the normal process of labor.

There is a definite tendency in the literature toward more active obstetrics, the value of which is very doubtful, notably outlet forceps operation, routine version and extractions, routine breech extraction, induction of labor in every case at term, and particularly rupture of the bag of waters for the induction of labor or to hasten the progress of the first stage. Some of these procedures when done by their proponents in strict accordance with the proposed indications and conditions may yield satisfactory results. However, the influence of this teaching on the less expert members of the medical profession tends toward more active interference with labor, which results in unwise application of these methods, very often with disastrous results. The continued practice of this teaching can only effect a tendency away from natural labor.

INDUCTION OF LABOR

The exact cause of the onset of labor is not known, but it is well recognized that the nearer a pregnancy is to the time that labor would start spontaneously the easier

it is to induce the onset of labor. Our methods, however, for determining how close a patient is to the termination of her pregnancy are crude and uncertain. Furthermore, there is at the present time no satisfactory method for the induction of labor. That most widely used is quinine and castor oil and, as generally applied, this will induce labor in exact proportion to the proximity of the pregnancy to term. But quinine has been charged with the death of infants in patients sensitive to the drug. A few cases have also been reported in which quinine is believed to have contributed to the rupture of the uterus. Its use has been abandoned in some clinics.

The use of quinine, castor oil, pituitrin and the Voorhees bag is not without danger. Their application is never indicated except when the reasons for the induction of labor are important enough to outweigh the objections to their use. The induction of labor by any method for the convenience of either the doctor or the patient cannot be too strongly condemned.

When an attempt is made to induce labor, the doctor will usually begin with the less radical methods. If these attempts fail, it becomes a matter of pride to succeed in his undertaking and he proceeds with each method more radical than the preceding one, burning all his bridges behind him. After days of uncertainty, the case terminates with a dead baby and an exhausted mother. To assume the responsibility for a possible outcome such as this, one needs a real reason for the undertaking.

It is inconceivable from a biologic standpoint that the bag of waters is of no value in the mechanism of labor. No one will deny that the bag of waters offers a protection to the baby in an actively contracting uterus. There is a variable limit to the length of time a baby can survive after rupture of the bag has occurred. It may be impossible for the fetus to be safely delivered before this time has passed. Prolonged labor from inefficient uterine action can never be prognosticated with certainty. The outcome not only for the baby but for the mother as well, in this difficult complication of labor will often be determined by the length of time the bag of waters remains intact. In a large clinic with a proportionate number of prolonged labors, the importance of an intact bag of waters is frequently observed. Although the so-called "dry labor" frequently terminates as a natural labor, there is a certain definite number of cases in which rupture of the bag of waters plays a major rôle in the death of the baby. The promiscuous and routine procedure of rupturing the bag of waters for the purpose of inducing labor or shortening the first stage of labor is a very questionable practice and will in a certain definite proportion of cases convert natural labor into an abnormal labor.

BREECH

The practice of "breaking up" the breech as a routine procedure is gaining in popularity in various clinics throughout the country. This is an example of the trend of obstetric teaching away from natural labor. The hazard to the baby is inherently greater in breech presentation than in cephalic presentation. A large number of breech cases will deliver spontaneously to the umbilicus, so that this presentation may be classed with natural labor.

Although long series of cases have been reported in which the mortality in breech extractions has been lower than in spontaneous delivery of the breech, it must be remembered that these cases were handled in a hospital under supervision of expert obstetricians. These results are not comparable with those to be expected in the hands of the general practitioner who is not under supervision and who delivers only two to four breech cases a year, and who, because of his limited experience, cannot be expected to carry out an often complicated procedure with success. In a series of 16,000 consecutive deliveries at Cook County Hospital, there were 604 spontaneous breech deliveries with a corrected

mortality of 3.8 per cent. There were thirty breech extractions with a mortality of 16 per cent. It is believed that the conservative attitude in respect to breech presentation, which allows a natural labor to remain natural as long as possible, is responsible for this low mortality.

ROUTINE VERSION AND EXTRACTION

Not many years ago a furor for the performance of routine version and extraction swept the medical profession throughout this country. Fortunately, the enthusiasm was short-lived because of the devastating results for mother and baby. This procedure is perhaps the most noticeable example of the crude efforts to improve upon the expert performance of nature. Version and extraction, to be reasonably safe, must be done with a most accurate compliance with the conditions laid down in every textbook, and for reasons sufficient to justify the performance of an operation which in itself carries a high mortality and morbidity.

ROUTINE FORCEPS DELIVERIES

For a great many years, obstetricians have shortened the second stage of labor by an outlet forceps operation. This was contrary to the old teaching which advocated the use of forceps only when necessary. In recent years this method has been given the stamp of approval by an increasing number of teachers of obstetrics, until at the present time in many hospitals it is almost a routine procedure.

It has been stated on good authority that the incidence of cerebral hemorrhage is lower in cases which are delivered by means of outlet forceps and episiotomy than when the head is allowed to deliver spontaneously. From a mechanical standpoint it is difficult to understand how a head dragged by forceps through a vagina enlarged by an episiotomy will receive less traumatism than a head forced through the same opening by the powers of labor. The success of so many outlet forceps operations is an indication of the amount of insult a child's head can survive rather than a credit to the art of obstetrics.

Outlet forceps delivery performed with the conditions actually present, namely, perineum beginning to bulge, complete anterior rotation, and episiotomy, is in itself the least objectionable of all the procedures which have been discussed. However, the routine application of this method, which frequently requires that a patient making normal progress toward a natural delivery be put to sleep and delivered with forceps, differs only in degree from the method that under the same circumstances pushes the head up out of the pelvis to do a version and extraction. It must be remembered that many errors are made in the diagnosis of the degree of descent of the head in the pelvis, and many doctors fail to distinguish the difference in forceps operations with respect to the amount of descent and degree of rotation. Therefore, if routine outlet forceps delivery is generally taught, there will be a tendency to extend the application of the forceps to cases above the outlet with a still greater increase in maternal and fetal injury.

THE THIRD STAGE OF LABOR

The third stage of labor perhaps offers more opportunity and temptation to interfere with natural labor than does any other stage. Although the student is taught with all force possible that the "hands off" policy with intelligent management will result in the least loss of blood and the fewest complications in this stage, when he is left to himself, he will yield to the temptation to manipulate and massage the uterus in a usually futile attempt to hasten the delivery of the placenta. Every sin of commission that can be imagined is commonly practiced to hasten the progress of the third stage. To the human mind the third stage seems to be incompatible with noninterference.

The objective in the third stage is to secure a spontaneous delivery of the

placenta with a complete and untorn maternal surface and with the smallest blood loss. To attain this objective it is imperative for the attendant to await patiently the process of natural labor until the placenta is separated, whereupon it will be delivered spontaneously, or may be expelled by simple and harmless assistance. Manipulating the uterus, early attempts at Crede expression, before placental separation, positively interfere with this mechanism and are not only unnecessary but cause complications which result in bleeding and delay the delivery of the placenta.

CONCLUSIONS

During the last two decades the death rate in the first year of life has been markedly reduced. This reduction has occurred almost entirely after the neonatal period. With the recent increased attention given to prenatal care, there has been some small decrease in the number of deaths from conditions which can be influenced by better management during pregnancy. As the study of this question continues the light of investigation is being focused more and more upon the delivery room. Further improvement in infant mortality must be accomplished by reducing the hazards to mother and infant during labor. Since natural labor involves the least risk, it is obvious that nothing should be done that will change a labor that could be natural into an abnormal labor.

It is true that a relatively small number of pregnancies and labors will be abnormal and require intervention of one kind or another. These pathologic cases, however few in number, require skill and judgment beyond those usually acquired by a doctor whose obstetric practice constitutes only the smaller amount of his work. In a hundred obstetric cases, ninety-five are of such a nature that the experience gained in their management is of little or no value to the doctor when he is confronted with a major complication of obstetrics. The answer to this problem presents numerous difficulties. Perhaps one could visualize a plan whereby in every community in the United States two or three physicians, especially trained in obstetrics, would be available for the aid of the general practitioner in managing this small percentage of his routine labor cases.

The practice of obstetrics seems to have been subjected to more criticism from the outside than any other branch of medical practice. There is no doubt that further improvement in the practice of obstetrics can and will be accomplished. But it is to be hoped that any faults will be recognized and problems solved by the medical profession rather than by outside agencies, to the end that childbirth will be made even more safe in the United States.

FACTORS INFLUENCING THE SAFETY OF PAIN RELIEF IN LABOR*

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OPINION regarding pain relief in labor is in a chaotic state. Medical literature relating to obstetrics and to anesthesia contains endless controversial discussions regarding which combinations of agents and which methods of pain relief are most satisfactory. Obstetricians are being criticized because of the high incidence of operative deliveries, high fetal mortality rate, excessive maternal morbidity and mortality, and, more recently, because of the occurrence of permanent damage to the nervous system of the newborn child. All these circumstances are looked upon by some critics as sequelae of efforts at complete relief of pain. A glaring omission in the literature is the failure to emphasize the necessity for intelligent supervision of the physiologic activity of mother and child. In other words, it has apparently been assumed that administration of adequate quantities of pain relieving drugs to mothers in labor, constitutes the necessary extent of service.

In what follows, we wish to emphasize the necessity for careful physiologic management of mother and child during whatever periods of drug depression are thought justifiable. In other words, we hope to make clear the necessity of a competent anesthetist as a member of the obstetric team whenever an attempt is made to eliminate completely the pain of labor. The need for careful supervision of the mother and child progresses as the ideal of painlessness is approached. A large group of drugs, constantly growing larger, is utilized to promote comfort in childbirth. All are administered with the hope of producing sleep, amnesia, analgesia or anesthesia. The agents available, whether administered by injection, by inhalation, or through the alimentary tract, all produce undesirable and sometimes unrecognized side effects detrimental to the welfare of both mother and child.

DRUG EFFECTS OTHER THAN PAIN RELIEF

Disturbance of Reflexes. The autonomic nervous system is easily thrown out of balance by drugs which relieve pain. Either obtundation or hyperactivity of reflexes may be the result. No physician can prophesy whether reflex disturbances will take place in a given patient from a particular drug and dosage. If the reflex mechanism of labor itself is abolished or made hyperactive, it is a problem easily dealt with by the obstetrician. If, however, the pharyngeal and laryngeal reflexes are obtunded, a foreign body may obstruct respiration. If at the same time the vomiting reflex is hyperactive, a condition presents which must be cared for at once if permanent damage to the unborn child or even the mother is to be prevented. Depression of cough reflex promotes the chance of later chronic obstructive phenomena while reflex vocal cord adduction may result in acute oxygen want, dangerous or even fatal to the fetus. Depression of ciliary activity of the respiratory tract is now a recognized effect of the pain relieving drugs. How such action may affect the newborn is yet to be determined.

Muscle Relaxation. Loss of muscular tone of the mother during labor may, of course, decrease the effectiveness of expulsive effort. More important to the welfare

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of the baby, however, is the possible interference with respiratory exchange due to relaxation of tongue and pharyngeal mus-

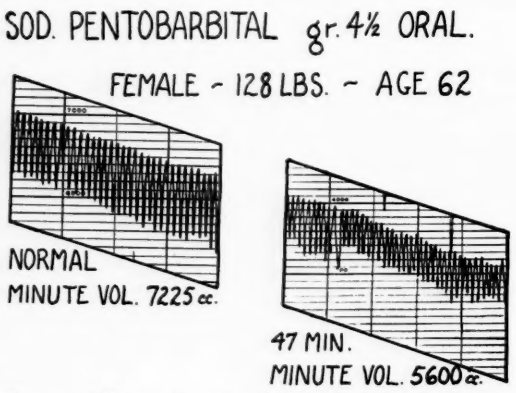

Fig. 1. Effect of oral administration of 4½ gr. (290 mg.) sodium pentobarbital upon respiratory exchange. Similar records made before and after administration of other nonvolatile agents show, with only two exceptions, similar reduction in respiratory efficiency, the reduction increasing with increased dosage and the susceptibility of the patient. Scopolamine hydrobromide and paraldehyde have little or no tendency to decrease respiratory exchange.

cles and the resulting encroachment upon the air spaces. Such respiratory obstruction is particularly apt to occur late in the second stage when more profound drug dosage is necessary, and when the result may be a poorly oxygenated respiratory center with its attendant failure to maintain function at birth. Even the most experienced anesthetist finds it difficult to recognize, by observation alone, respiratory obstruction of a degree quite capable of causing signs of oxygen want in the fetus.

Psychic Depression. Loss of conscious coöperation of the mother handicaps obstetric procedure in making aseptic technique difficult and in depriving the obstetrician of voluntary aid in expulsion. Less frequently is it appreciated that a woman with absent or fogged mental faculties may fail to turn her head, change her position or otherwise safely supervise her condition when vomiting or other threat to safety occurs.

Depression of Respiratory Center of Mother and Baby. Opiates, barbiturates and other nonvolatile drugs, as well as inhalation agents in sufficient dosage, all cause depression of the respiratory center of mother and child. Rarely can doses of nonvolatile agents adequate for pain relief be administered without measurable decrease in minute volume pulmonary ventilation. (Fig. 1.) A most potent depressant of cell activity is oxygen want. At the moment of delivery, the child's respiratory center is usually subject to at least some depression from drug action and from trauma. If at the same time, blood low in oxygen bathes the respiratory center, depression is further enhanced.

Technical Faults. Untoward results following improper management of the period of drug depression are, of course, largely dependent upon the four extraneous pharmacologic characteristics considered above. Nevertheless, further consideration of the technical difficulties of maintaining normal physiology may not be amiss. The ease with which vomitus may be aspirated is not generally appreciated. If the circumstance is recognized at once and properly treated, little harm may result. A minor degree of respiratory obstruction may be difficult or impossible for the inexperienced physician to recognize or to relieve. The degree of interference with gaseous exchange from obstruction of the air passages becomes comparatively more important as the total minute volume is less due to the presence of central respiratory depression. The need for prompt and sure relief of obstruction and restoration of oxygen is imperative. (Fig. 2.) During the administration of inhalation agents of slight potency, such as nitrous oxide, the temptation to permit mothers to inhale oxygen-deficient atmospheres is always present. Even during periods of milder drug effects, such as those accompanying administration of moderate doses of nonvolatile agents during the first stage, the safety of mothers and particularly of children can best be assured by the attention of well trained and experienced physicians who have mastered the art as well as the science of pain relief.

The presence of fetal movements in utero, the fetal heart rate and the presence

or absence of meconium in the outlet discharges are the three criteria at present available by which we may judge the condition of the unborn child. Since the pulse rate is particularly sensitive to oxygen deficiency, a means whereby it may be under constant observation during the second stage of labor is important. The delay involved in reporting by word of mouth from an observer to the anesthetist during the second stage has been found unsatisfactory and unsafe. The equipment shown in the illustration (Fig. 3) has been found satisfactory in putting the anesthetist in possession of essential knowledge for: (1) controlling the oxygen content of the mother's inspired atmosphere so as to avoid fetal anoxemia; (2) directing the expulsive efforts of the mother; and (3) well timed administration of inhalation agents while the head is passing the outlet.

Marked change in fetal heart rate has long been among the criteria indicating rapid delivery. Such change may, of course, be neurologic in origin. It may also be due to an uncontrollable circulatory defect. Not infrequently, however, both in the first and second stage of labor have we been able by well timed and adequate administration of oxygen rich atmosphere to the mother, to restore the fetal heart rate to normal and eliminate the need for forced delivery. An example of such control is illustrated in the accompanying chart. (Fig. 4.)

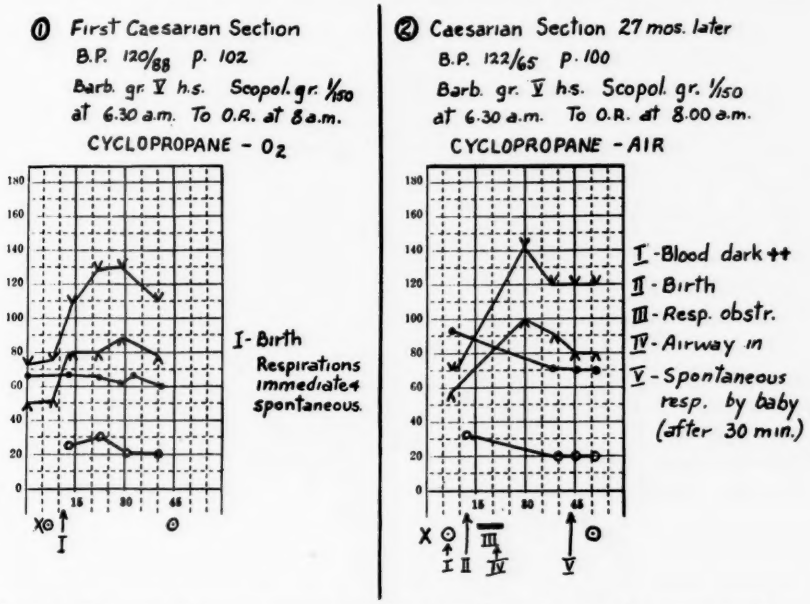
① First Caesarian Section
B.P. 120/88 P. 102
Barb. gr. V h.s. Scopol. gr. 1/150
at 6.30 a.m. To O.R. at 8 a.m.
CYCLOPROPANE - O2
I - Birth
Respirations
immediate &
spontaneous.
② Caesarian Section 27 mos. later
B.P. 122/65 P. 100
Barb. gr. V h.s. Scopol. gr. 1/150
at 6.30 a.m. To O.R. at 8.00 a.m.
CYCLOPROPANE - AIR
I - Blood dark ++
II - Birth
III - Resp. obstr.
IV - Airway in
V - Spontaneous
resp. by baby
(after 30 min.)

Fig. 2. Records of two cesarean sections performed upon the same mother. Condition of mother the day before and medication on both occasions were similar. (Code: V____V = blood pressures; ●——● = mother's pulse rate; ○——○ = mother's respiratory rate.) Intense fear was present when the woman came to the operating room on each occasion and was the apparent cause of low blood pressure and small pulse pressure on each occasion. In the first instance, cyclopropane was administered with excess oxygen and a smooth induction occurred, with restoration of mother's normal circulatory condition as soon as she was anesthetized. The baby cried spontaneously. In the second instance, cyclopropane in an atmosphere without excess oxygen was used. Induction was rough with severe respiratory obstruction. Mother's blood was cyanotic when incision was made. Restoration of a free airway, good oxygenation and probably of normal maternal blood pressure relations was not accomplished until eight minutes after the cord had been severed. Strenuous efforts were necessary over a period of a half hour before the baby's respiration was established.

DISCUSSION

It is obvious from the foregoing that agents which relieve pain have certain

secondary effects always tending toward interference with efficient respiratory exchange in the mother. The system of transport by which oxygen is conveyed from the atmosphere breathed by the mother through her alveoli, blood vessels and heart, to the placenta and thence through the fetal circulatory system to fetal tissue cells is a complicated one indeed. The elimination of carbon dioxide is no less intricate. Any respiratory or circulatory defect in the mother, any physical embarrassment to the cord, even the physical changes incident to uterine contraction, all these are potent sources of embarrassment to this transport system. The full extent of the influence of these extraneous characteristics of pain relieving drugs upon

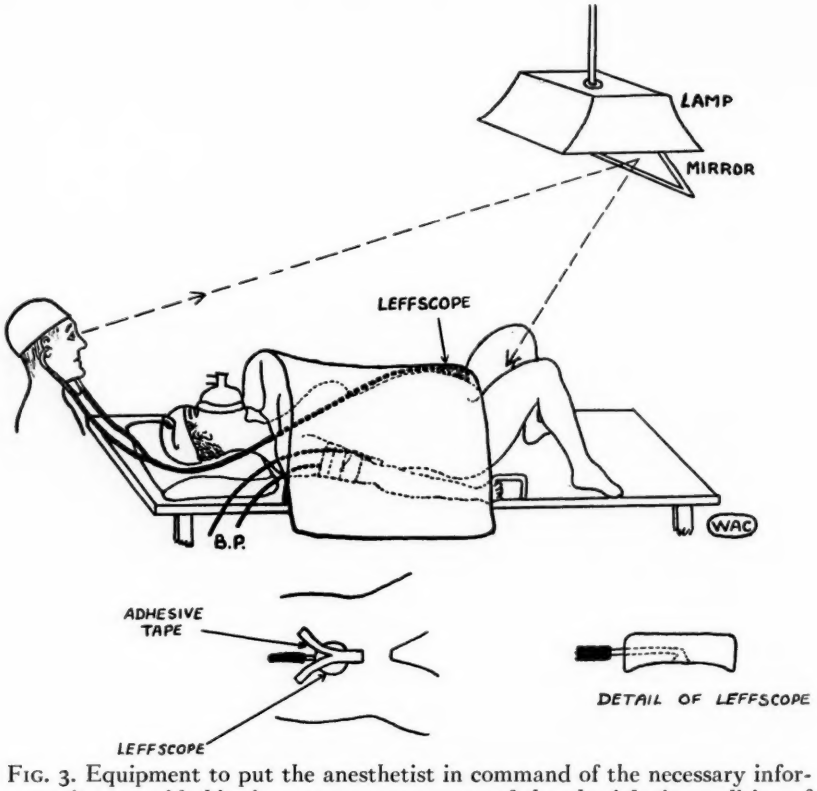

Fig. 3. Equipment to put the anesthetist in command of the necessary information to guide him in proper management of the physiologic condition of mother and child during second stage: Stethoscope bell is heavy metal (diameter 7.5 cm., weight 930 Gm.), no diaphragm, boilable, and has given satisfactory auscultation of fetal heart sounds during several years' use (Leff, M. *Am. J. Obst. & Gynec.*, 20: 108, 1930). Stethoscope and cuff on arm for observation of maternal blood pressures. A mirror attached to lamp frame by adjustable ball and socket joint makes perineum visible to anesthetist throughout expulsion.

Concentration of anesthetic gas or vapor can be varied to suit the needs of various individual types of contractions. Evidence of when to increase concentration is gained from three sources: the mother's impression, the anesthetist's hand palpating the abdominal wall, and from the mirror.

Marked changes in fetal heart rate can often be rectified by judicious enrichment with oxygen of the atmosphere inhaled by the mother. Excess oxygen, if properly timed, need not interfere with proper pain relief even when nitrous oxide is the sole agent in use. If the anesthetist palpates the abdominal wall and observes through the mirror late in the second stage, he can assist the obstetrician by encouraging or restraining the mother's voluntary effort according to the obstetrician's desires. Transmission of information by word of mouth from the obstetrician or his assistant to the anesthetist is too slow to permit the sudden changes in activity which are essential.

the initiation and maintenance of respiration of the child after birth, is not yet completely understood.

be conversant with the pharmacology of pain relieving drugs, their administration and the technical means of counteracting

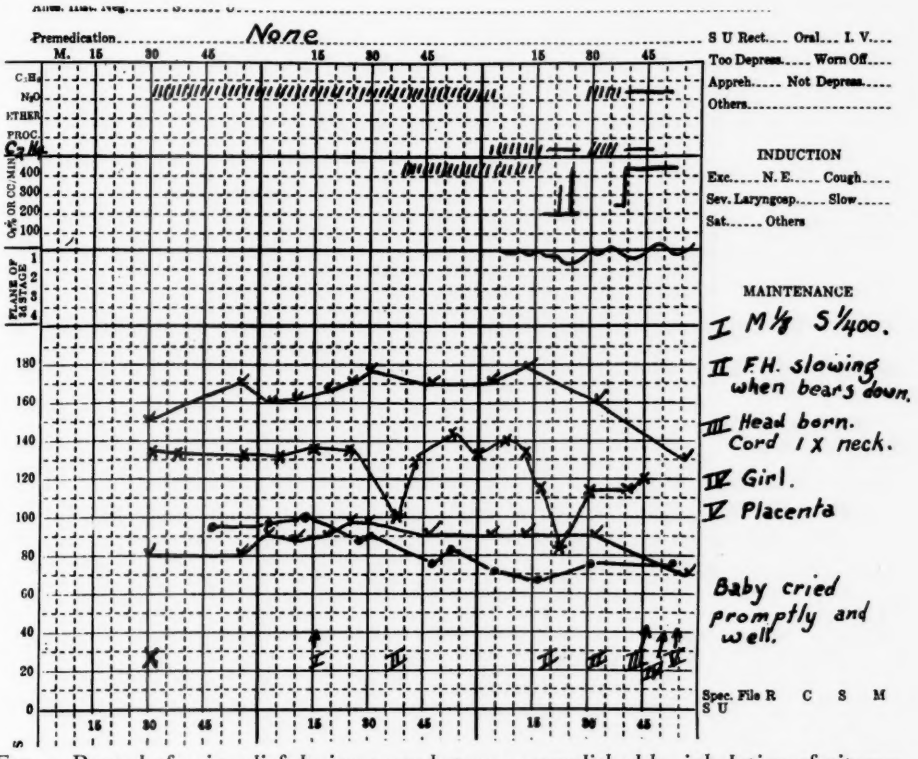

Fig. 4. Record of pain relief during second stage accomplished by inhalation of nitrous oxide-oxygen and ethylene-oxygen. (Code: V——V = systolic and diastolic blood pressures of mother; ●——● = pulse rate of mother; ×——× = pulse rate of fetus.) Many observations of fetal heart rate were made that were not recorded. The tendency is seen in the record, however, for the pulse to decrease in rate on certain occasions. The anesthetist observed that the maximum decrease in pulse rate occurred during and following the height of uterine contraction, when simultaneous lower concentration of oxygen was being inhaled. Administration of pure oxygen as soon as the uterus relaxed after each contraction was capable of presenting the decrease in fetal heart rate. The baby was born spontaneously over an hour later and cried immediately. Not infrequently have we seen similar evidence of oxygen want in the fetus (decreased heart rate) during the first stage, relieved by administration to the mother, between contractions, of oxygen-rich atmosphere or pure oxygen gas.

It is well recognized that, even when no drugs are administered to the mother, transit through the birth canal is a hazardous journey. Interference with oxygen and carbon dioxide transport is recognized as not the least of the dangers. It is our belief based on clinical experience that if complete pain relief in labor is to be our aim, a physician thoroughly conversant with the physiologic mechanism of gas transport and methods of aiding and correcting it, should be a constant member of the obstetric team. If the pain of labor is to be safely and completely abolished, such a physician should their undesirable side effects. The surgical profession has accepted the fallacy of the belief that the surgeon can spread his attention to cover pain relief for his patient, supervise the welfare of the patient and yet offer the best that he has of surgical skill. In obstetrics, two patients are concerned. The transport system for oxygen and carbon dioxide is more complicated. If we are to aim at safe and efficient pain relief in obstetrics, we must admit the anesthetist to the obstetric team. To fulfill his function, such an individual must recognize wherein the problem of pain

relief in obstetrics differs from the similar problem in surgery. Observation and supervision of the condition of the fetus in utero and its mother is perhaps more difficult than is similar service for the surgical patient, at least it is different. Few surgical anesthetists have devoted sufficient attention to the obstetric problem to perfect themselves in it.

In one American city a well trained anesthetist has for several years specialized in obstetric anesthesia. This plan has proved satisfactory to him both economically and professionally as well as to several obstetricians and their patients. His work is confined largely to one lying-in hospital. In coöperation with the obstetricians, he supervises dosage of nonvolatile agents during the first stage of labor. He is responsible for observation and care of mother and fetus while they are affected by drugs. These duties are sandwiched between administration of volatile or gaseous agents during second and third stages of labor; thus he is available at all times to recognize at once disturbed physiology in mother and fetus or newborn and to rectify or treat promptly physiologic disturbances. Such a plan may be found a future solution of many of the obstetrician's difficulties.

CONCLUSIONS

In America in recent years we have indulged too much in the hope for a possible drug or combination of drugs which may be expected to abolish safely all pain in connection with childbirth. We have looked upon new and untried drugs as the solution of our difficulties when we might better have devoted our efforts to a search for better ways of using agents with which we are already, at least partly, familiar. We have neglected to a large extent consideration of disturbances of physiologic balance in mother and child which are and always will be necessary accompaniments of administration of all drugs which relieve pain.

The authors believe that if complete safety and complete pain relief are to be our aims, we must admit that the two objects *tend* to be reciprocally incompatible—more safety, less pain relief; more pain relief, less safety. We believe our aim ought to be the most complete abolition of pain compatible with perfect safety to mother and child during labor and thereafter. If such is the aim of obstetric practice in America, pain relief must wait upon safety. If practical considerations for the present preclude the services of a physician well trained in both the science and the art of pain relief, drug administration must be limited, and pain relief must be limited, to an extent compatible with the knowledge, skill, and experience of the physician in charge. The doctor must appreciate that the more familiar he is with the effects of drugs which he uses, the more likely will he be to treat properly disturbances which result from drug effects. Taking up the use of a new drug or combination of drugs because some one else reports success with it is a dangerous experiment to be undertaken with care. The safeguards efficacious with one method are often futile with another.

We would admonish the practitioner not to forget that ether, chloroform or nitrous oxide combined with appropriate mental suggestion, have in the past in the hands of those skilled and experienced in their use, offered great satisfaction and safety to many mothers and children. The same may be said of opiates and scopolamine. The skill, knowledge, experience and attention of the physician, devoted to the dosage of a particular drug or combination of drugs, and methods of correcting promptly all ill effects, shall be the gauge by which is determined the extent of pain relief legitimately to be sought for in a given case.

VERSION AND BREECH DELIVERY*

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DEFINITIONS

VERSION means turning. Obstetrically it means changing the part of the fetal ovoid which presents at the pelvic inlet. It is named respectively for that end of the ovoid which presents at the completion of the maneuver. Thus it is cephalic if the head end of the fetus is caused to present, podalic if the buttocks and/or lower extremities are caused to present. Only the latter will be discussed here.

The turning is in itself a complete maneuver; it does *not* include the extraction of the baby after it is accomplished. While in most cases extraction is an immediately sequential procedure, it need not, and in some cases *must* not, be so carried out.

We shall have no reference herein to so-called "elective podalic version."

There are several varieties of podalic version, named respectively in reference to the technique employed. That referred to herein is the "combined" variety accomplished by simultaneous manipulation within the uterus, and outside the abdomen.

INDICATIONS

Since, as will be seen, it is never desirable to have the podalic end of the fetus present, podalic version is done only for some direct objective more urgent than the general desirability of the more favorable cephalic presentation.

Chief among such indications are: faults of presentation, as many cases of transverse presentation; some impacted face or brow presentations; some compound presentations; occasionally, as in twins, normal cephalic presentation, where conditions for the operation are easy and expedition of delivery is legitimately indicated.

Formerly almost the only resource in such situations, version has been superseded in many cases by cesarean section. It should today be reserved for those cases in which the fulfillment of proper indications for its employment permits its use with nominal risk. It is used here primarily in the mother's interest. Therefore, it should not be selected when it represents greater risk to her than the dilemma from which extrication is sought.

In prolapse of the cord, the operation may be employed, primarily in the interest of the fetus. But it is generally without avail in that interest unless the labor may thereby be *quickly* terminated. Only where its conditions are ideal, may it be used to finish labor rapidly without great risk to the mother. In any other situation, therefore, in which the cord prolapses and cannot be replaced, and the labor cannot be managed deliberately, it is better to accept the loss of the baby rather than to subject the mother to great risk of danger in performing version.

Version still has a distinct place in the treatment of placenta previa, though here

* From the Margaret Hague Maternity Hospital.

also the hydrostatic bag and cesarean section have partly supplanted it. It is especially when used for this condition that immediate extraction is dangerous and contraindicated.

While general conditions of the mother not infrequently make desirable the rapid termination of labor, it is relatively very rare that version will constitute the procedure of choice to accomplish it.

The employment of version in cases of impaction of the head in the inlet by relative cephalopelvic disproportion is debatable. It was formerly importantly depended on in such situations, even in high degree of disproportion. And there is no doubt, as a matter of experience, that it has many times successfully solved such difficulties. But since it is inevitable that in many such cases ideal conditions for its employment will not obtain, recognition of the danger to both mother and child has tended to lessen its use. Cesarean section will properly supplant it in some cases. Expectancy and forceps will, in our opinion and experience, supplant it in nearly all the others.

There are two principal techniques used in version. That of Braxton-Hicks is done by restricting the intra-uterine manipulation to the introduction of two fingers through the imperfectly dilated os cervicis, bringing down one limb only, and desisting after this is accomplished. The prolapsed half breech acts as a tampon against, and dilator of, the lower uterine segment. It is a difficult procedure, is applicable *only* to certain cases of placenta previa, and is today rarely used, having been supplanted by other methods.

The second technique involves the introduction of the whole of the internal hand into the uterus. Conditions for this procedure are, ideally, that there shall not be cephalopelvic disproportion, that the cervix be fully dilated, that the membranes be unruptured, that there be no placenta previa, that the uterus be not hypertonic nor already injured. Under these conditions we believe that Potter's technique is not surpassed.

The patient is deeply anesthetized to produce uterine relaxation; the internal hand, the palm of which faces the baby's belly, is introduced gently between the uterus and membranes, stripping the latter up gently without rupturing them. The placenta, if approached, is of course avoided. The head is disengaged and pushed to the side toward which the back lies, at the same time that the external hand pushes the breech to the opposite side. The arms are felt and if necessary effort is made to fold them properly in against the chest. The uterus being relaxed, and the fetus floating in the amniotic fluid, the manipulation described brings the belly and limbs of the child dependent. The membranes are now ruptured and *both* feet seized and brought down through the cervix. Under these conditions, extraction may be carried out forthwith. Gentle, steady traction downward and backward is made on the legs and thighs. The breech will tend to come down posteriorly. But after it is delivered, continuation of traction in the same direction will tend to rotate the torso spontaneously and one or both shoulders will swing under the symphysis. *No pressure* on the fundus should be made during this process. Not until one or both scapulae appear beneath the symphysis is attempt made to deliver the arms. Then stroking of the exposed anterior scapula toward the midline of the baby's body will generally disengage the arm. By slight rotation of the torso and a repetition of the maneuver the other arm is delivered. Then, with the internal hand flexing and guiding the head, the outer hand making gentle traction on the shoulders, and the assistant now gently pressing and guiding the head into the inlet by suprapubic, not fundal, manipulation, the head is extracted.

Necessitous version will, however, frequently have to be done when membranes are ruptured, when the head is rather tightly wedged into the inlet, when an arm is prolapsed, when the uterus is tonic and clamped down on the fetus. Its perform-

ance under such conditions must always be most seriously weighed, and avoided if possible. But if it must be done, the technique is much more difficult and must vary from that described as conditions make necessary. The prolapsed arm must be secured, as a rule, by a sling before proceeding. Again, deep anesthesia is essential to relax the uterus. But the baby will not float freely in the amniotic sac. Patient, gentle, prolonged manipulation may be needed to disengage the head from the lower segment. Both feet may not be accessible, and only one, preferably the anterior, may have to be brought down; even this may require placing a fillet on the ankle before it can be accomplished. Arms, in spite of care, may extend, or wrap themselves around the neck and require patient deft work to disengage them.

Anticipating troublesome possibilities, prior provision should in every case be made of hot moist towels to protect the baby during extraction; of abundant sterile green soap for lubrication incident to all manipulation; forceps to use should the aftercoming head be impacted; oxytocics to control inertia; facilities for cervical repair; means of efficient fetal resuscitation; donors and apparatus for blood transfusion; equipment for craniotomy should the baby succumb during the operation and the head be stubbornly impacted.

The operation is a dangerous one. For the baby, there are the dangers of all breech extractions, besides those sometimes inherent in the maternal indication for the operation. For the mother, there are the dangers of the original indication in some cases plus the grave risk of lacerations of the cervix, the uterus, and contiguous tissues. There is no method of delivery save cesarean section which so thoroughly invades the uterus. The infective danger inherent in such invasion always attends this operation.

We have analyzed 221 cases of combined version from our clinic. Table 1 exhibits the indications and the results in mortality.

Table 1
COMBINED VERSION
(None Elective)

Indication	Number	Maternal Deaths	Per Cent	Fetal Deaths	Per Cent
Extraction of second twin	45	0	...	1	2.2
Transverse presentation	41	1	2.4	13	30.0
Placenta previa	35	1	2.9	16	41.0
Prolapsed cord	31	0	...	11	35.0
Impacted cephalic presentation	25	0	...	8	32.0
Face presentation	12	0	...	3	25.0
Abruptio placentae	11	0	...	8	73.0
Prolapsed arm	9	0	...	5	44.0
Toxemia after bag induction	8	0	...	1	12.5
Brow presentation	5	0	...	2	40.0
Totals*	221	2	0.9	68	30.8
	177	2	1.1	67	38.0

* If the practically elective use of the operation for expedition of delivery in twin pregnancy is eliminated, the totals would be as shown on the lower line.

The tremendous fetal mortality was, of course, not directly due to the operation. Prematurity and the effects on the babies of the primary conditions, such as separation of the placenta, prolapse of the cord, placenta previa, were chiefly responsible for the mortality. It probably could not have been very significantly lowered by different handling. However, 25 per cent of the fetal deaths were definitely due to intracranial hemorrhage; one craniotomy was performed; in one case there was traumatic infiltration of kidney and adrenal. All these were attributable to the operation.

Table II
MATERNAL COMPLICATIONS

Severe postpartum hemorrhage	16	
Definite laceration of cervix	15	
Endo- and parametrial infection	6	
Rupture of uterus	3	30
Total serious morbidity		13.6 per cent

All maternal complications (Table II) may be attributed to the operation, as those hemorrhages dependent on conditions for which the procedure was employed are eliminated. One of the two maternal deaths, a rupture of the uterus, is directly chargeable to the operation.

Version, as initially defined herein, is an operation of venerable antiquity with a most respectable record of great usefulness;

calling upon the best technical capacity of the obstetrician in performance; capable of brilliant and satisfactory results when properly employed; but embodying great dangers and therefore requiring the most careful and experienced judgment in its application.

BREECH EXTRACTION

Breech presentation is that condition in which the breech or buttocks end of the fetal ovoid first approaches the pelvic inlet at the onset of labor. Of its varieties, "frank breech" presentation designates the extended relation of the legs to the fetal body; "footling" the flexion of the legs on the thighs, with or without extension of the thighs, so that the foot or feet precede the buttocks in their passage of the inlet, or come down with them.

If all conditions are favorable, breech presentations, like cephalic, are capable of spontaneous delivery. The obstetrician will, when the termination of spontaneous delivery is imminent, *manage* the delivery, in regard to protecting the perineum, employing episiotomy where indicated, maintaining head flexion, protecting the cord, making traction on the shoulders, and guiding the extrusion of the arms, exactly as in his management of vertex deliveries. This does not constitute interference with a normal process, or "assistance" in any special sense. The term "assisted breech delivery" is in our opinion loosely defined and meaningless.

If there are factors of obstruction to the passage of the fetus, interference, as by manual correction of relation of parts, manual or forceps traction, and so forth, will be necessary as in similar situations in relation to cephalic presentations. These all constitute operative interference, and should be designated by appropriately descriptive terms.

Inasmuch as the great preponderance of cephalic presentations is determined by the resistances of the normally tonic uterus applied to the fetus, any influence which alters these factors, such as flaccidity of the uterus, over-distention thereof by polyhydramnios or multiple pregnancy, distortion of its cavity by tumors or placenta previa, abnormalities in proportion of the fetus, is prone to cause breech presentation. It may even occur where no ascertainable cause can be assessed. It occurs in earlier stages of pregnancy in many cases which later present by the head. This accounts for the high proportion of breech presentation in prematures.

The mechanism of labor in breech presentation tends to present exactly the same phenomena as in cephalic presentation. However, as the dorsolumbar portion of the fetal axis is not so conveniently jointed as the cervico-occipital portion, the evolution of this mechanism is not so perfect in breech as in cephalic presentation. This fact, together with the relative inadequacy of the soft amorphous breech as a dilator, in comparison with the firmer, better shaped head, makes these presentations more tedious and difficult for the mother.

They are especially hazardous for the fetus for three principal reasons. First, as stated, they frequently attend other abnormalities unfavorable to fetal survival, especially prematurity. Again, delay in the delivery of the head after that of the torso induces asphyxia because the fetus is, in general, unable to respire during this interval. This situation has no parallel in cephalic delivery. Finally, and most important, the liability to intracranial damage is much greater in aftercoming than in forecoming heads. This is because all the pressure necessary to mould the head has to be compressed into a few minutes instead of being spread over several hours. It is the difference essentially between concentrating a certain amount of force or trauma into the equivalent of a sudden blow, and spreading it out in a series of relatively gentle intermittent pressures.

In the management of breech presentation, external cephalic version has prophylactic worth. There is some difference of opinion as to the optimal time for this

effort. We think the completion of the thirty-sixth week is best. It can be successfully accomplished in approximately 60 per cent of cases. It must always be *most gently* done and the fetal heart action must be closely watched. It is best to do it without anesthesia, so that the patient's subjective discomfort may limit the force employed. *Don't hurt the patient. Stop at once* if fetal heart tones indicate distress. Try to rule out placenta previa before undertaking version.

If the case goes into labor in breech presentation, the management should in general embrace the same expectant attitude as in cephalic presentations. All preparations for emergency should be made as discussed under version. The perineum may be protected by episiotomy and by support of the breech as it is extruded.

When the breech is fully born, the legs, if extended along the torso, may be gently flexed and brought down. Deliver the upper torso and shoulders as described under version. Do not hurry this stage. While the safe time for completing delivery is actually limited, it is better to be gentle than to gain time by damaging, forceful haste.

The head in these situations never has had the advantage of partial moulding as it frequently has where extraction follows version, whereas the baby is usually full grown and in good condition. The manipulation of the head, therefore, calls for even more finesse than where version has been done. It should be well flexed, and brought through the inlet approximately in the transverse axis. Rotation of the occiput forward should be done only when the head is well down in the pelvic cavity.

If the passage of the inlet is not easy, prompt resort should be had to the application of forceps, rather than reserving this resource for attempted extrication of a head already badly traumatized by overzealous manual traction. The special forceps of Piper is a facile instrument, but any good type of forceps may be used. Once the face is exposed in the vulva so that access of air to the infant's lungs is established, there is no further necessity for haste and the resistance to the passage of the head over the pelvic floor may be deliberately managed.

In premature babies delivering by the breech, special caution should be employed. The relatively slender body sometimes slips through a poorly dilated cervix. Give the cervix time to dilate spontaneously. The slender chance of saving a questionably viable infant is not worth the risk of cervical damage consequent on hurried extraction.

In 20,000 deliveries in our clinic there were 859 breech presentations, an incidence of 4.3 per cent. Of these, 675 were full term. With reference only to the term cases, fifty-one babies were stillborn, while an additional twenty-five died in the neonatal period. In percentages, this is a fetal mortality of:

	Per Cent
Stillbirths	7.5
Neonatal deaths	3.8
Total	11.3

This compares with the average percentages of fetal mortality of:

	Per Cent
Stillbirths	2.41
Neonatal deaths	2.46
Total	4.87

The divergence well exhibits the increased fetal risk of breech delivery. This risk depends most on the direct mechanical injuries involved, i.e., intracranial hemorrhage, with or without fracture of the skull, and trauma to other viscera.

Forceps and cesarean section were the principal methods of operative interference, representing 19.5 per cent and 2.3 per cent incidence respectively. These figures are not significantly different from the incidence of these procedures in cephalic presentation. A craniotomy incidence of 1 per cent was, however, distinctly higher than the incidence in cephalic presentation.

There was no maternal mortality attributed to breech presentation per se.

SUMMARY

1. Podalic version is discussed without reference to its so-called "elective employment."

2. Its indications are detailed, showing that its use even for necessitous conditions is not so frequent as in the past, due to the availability of other delivery procedures.

3. The technique of its performance is briefly outlined, with emphasis on provision of resources for handling complications.

4. It is pointed out that the operation represents distinct hazards both to the mother and baby. Data of 221 cases are furnished, showing an average fetal mortality of over 30 per cent, principally stillbirths, which is more than ten times the stillbirth rate for the whole material of the clinic. One-quarter of this stillborn rate is due to intracranial damage. Maternal death is occasionally directly dependent on the operation. High incidence of grave maternal complications follows it.

5. Breech presentation, its frequency of occurrence, its principal causes, and certain principles of mechanism are discussed, and the hazards for the mother and fetus are outlined.

6. The management and technique of delivery are described.

7. The ratio of stillbirth and neonatal death incidence in this presentation are compared with the average ratio in the whole mortality of the clinic, and shown to be more than twice as high as the latter.

THE USE OF THE OBSTETRIC FORCEPS

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THE obstetric forceps, like the automobile, may be indispensable, if properly used, in the saving of life and human effort and suffering; and, improperly used, it may be the instrument of many unnecessary deaths. There are six principles essential to the safe and successful use of the forceps:

1. The cervix must be fully dilated, that is, its passage must be large enough to slip over the head at the plane of maximal diameters without retarding pressure. It is very easy to let one's obstetric conscience slip in this direction until, by degrees, it becomes habitual to apply the forceps when the cervical passage lacks 2 or even 4 cm. of complete dilatation. It should be remembered that a rim of cervix 1 cm. wide diminishes every diameter of the passage by 2 cm. Dragging the head through this inadequate opening results at least in laceration of the cervix, and at most, in fatal intracranial strains and resultant hemorrhage.

2. The forceps must be properly applied. It may be difficult (in rare cases, impossible) to apply the forceps symmetrically to the head, but repeated attempts should be made until the sagittal suture coincides with the vertical plane of the forceps. Failure to effect this adjustment accounts for most of the cases of slipping of the forceps. Properly applied, it is almost impossible (impossible within the justifiable limits of force of traction) to pull the forceps off the head. Improper application results in a mechanical maladjustment somewhat like using the wrong wrench on a bolthead—the wrench is almost certain to slip, or to hold only because of damage to the bolt. Pressure injuries to the soft parts of the fetal head may be inevitable; but gashes and tearing off of ears, lips, etc., should never occur.

3. Force in the application and adjustment of the forceps is never permissible. If difficulty is encountered, something is wrong—the position of the head has changed, the forceps has slipped outside of the cervix instead of inside it, the blade has caught against an ear or some other prominence, or the whole route of the introduction of the blade has been wrong. Proper introduction of the forceps involves a knowledge of the topography and axis of the birth canal, and requires a technique of letting the blade follow the line of least resistance (as in sounding of the urethra). Any attempt at forcible steering is apt to lead the top of the blade into a hopelessly blocked situation. It is better to dislodge the head and change its position than to attempt to force the forceps past any serious obstacle.

4. The head should never be compressed by squeezing on the handles of the forceps. It is very easy, in making traction, to apply great lateral pressure on the head by involuntary squeezing. Once a snug and accurate fit of the blades has been accomplished, nothing is gained by further compression: in other words, excessive compression adds no security against slipping.

5. Force in extraction should never be employed. It is difficult to estimate the tractive force which one employs in actual practice, so that dynamometric figures are of no great practical value. Force sufficient to move the patient on the table is excessive. Moderate traction will cause the pelvis to slide on the fat of the buttocks, so that, especially in obese individuals, the apparent to-and-fro movement of the pelvis may be quite great; but the buttocks

should never slide on the pad, nor the pad on the table. The whole secret of forceps-traction lies in a reproduction of the effect of a strong expulsive effort. To attempt to accomplish the second stage of labor in one terrific pull creates destructive stresses and strains on the intracranial architecture. Rather, one should aim, by repeated pulls, with a rest of at least a minute between each pull, to reproduce natural labor. This permits moulding to occur, and facilitates the natural adaptation of the head to the contours of the pelvis with resulting necessary changes in the position of the head. It is far better to expend an hour or more in securing an undamaged baby than to terminate the process rapidly at the cost of the baby's life. An effective safeguard against excessive traction is offered by having the operator sit on a stool without bracing his feet against the floor (to say nothing of bracing them against the delivery table).

6. The mechanics of forceps delivery must reproduce the mechanism of labor. This, of course, requires a knowledge on the part of the obstetrician for the diagnosis of fetal position; of the landmarks of the presenting part; of the pelvic contours at the various levels; of the necessary elements of rotation, flexion, and extension; and of the axis of the birth canal. In a brief paper, it is impossible to enter into the detail of all these elements. It must suffice to say that the exact position of the presenting part must be determined; that a proper cephalic application of the forceps must be made; that the head must be flexed and rotated until the plane of its maximal diameter lies in the most favorable relation to the diameters of the pelvic plane involved; that traction must be made in the axis of the birth canal; and that the elements of rotation, flexion, and direction of traction must constantly be changed as the head descends. Such a technique is very different from that all too commonly seen, in which the instrument is forced into some sort of a pelvic application, without any attempt to check up carefully after the application, and by which the delivery effected by continuous horizontal traction of a violence limited only by the physical strength of the operator.

Episiotomy. The role of episiotomy in connection with forceps is a dual one. In the application of forceps above the mid-pelvic level in malpositions, a preliminary episiotomy will often greatly facilitate the introduction and placement of the blades. Still more important is the commonly overlooked factor of the elimination of the added pressure upon the fetal head created by the dilatation of the introitus. Episiotomy is commonly regarded as a safeguard to the mother and yet the worst that can happen to her in the absence of episiotomy is an extensive reparable laceration, while the added pressure in perineal dystocia or in forceps extraction may cost the baby its life. In the major forceps operations, the traction and relatively rapid moulding has created an excessive intracranial strain by the time the head reaches the perineum; and the added pressure involved by using the head as an introital dilator may easily become the straw that breaks the camel's back.

Levels of Application of Forceps. There seem to be no generally accepted definitions of the terms "high," "mid," and "low" forceps. For the purposes of this discussion, the following definitions are used: "High forceps" means the application of forceps when the plane of maximal cephalic diameters (in the existing cephalic attitude —not necessarily the strict anatomic plane of maximal diameters) lies in the plane of the pelvic inlet. "Mid forceps" means the same in relation to the plane of maximal diameters and "low forceps" the same in relation to (or below) the plane of minimal diameters. There are of course, intermediate stations at which the forceps must be applied. For practical purposes, a rough estimate of the level of the plane of maximal diameters can be made from the level of the vertex, which lies more or less one station below the plane occupied by the plane of maximal diameters: in high

forceps the vertex is above the ischial spines; in mid forceps it is at the level of the spines; and in low forceps it lies against the pelvic floor or at the plane of the outlet. "Floating forceps" is an obsolete procedure, version and extraction being by far preferable.

1. The *low forceps* is the simplest application and hence may serve as a starting point. With rare exceptions the position is occipito-anterior within a range of about 30 degrees to either side of the sagittal plane. If the perineum has been somewhat distended, the sagittal suture usually lies in the sagittal plane of the pelvis. It must be remembered that with each recession of the head marked rotation may occur, especially as anesthesia is deepened for the actual application: hence it is necessary to re-orient the head at the moment of application of each of the blades, and to re-check the entire situation before and after locking the blades. With everything in order, traction is made as described in the first section of this discussion. The direction of traction varies with the level at which the plane of maximal cephalic diameters lies—at a point just below "mid forceps" the traction is outward and slightly backward; as the head impinges upon the perineum it is directly outward; and as the head distends the perineum and emerges from between the tubera the traction has more and more of a forward trend until, as the occiput slips from under the pubis, the traction is almost directly forward. If episiotomy is done, the perineal stage of labor is eliminated and the head is delivered by direct outward traction until the occiput slips out from under the pubis. If the perineum is allowed to remain intact, a great many operators remove the forceps from the head as the occiput disengages, and express the head through the introitus by pressure through the distended perineum from behind. My personal conviction is that the head is better controlled by not removing the forceps, and that the presence of the instrument (if properly managed) adds nothing to the risk of perineal laceration.

2. The *mid forceps* is almost always a "forceps operation of necessity," in contradistinction to the low forceps, which is usually "elective." Episiotomy will ordinarily eliminate the necessity for low forceps; but, since the mother must recover from the deeper anesthesia required for an episiotomy before the resumption of effective contractions and expulsive efforts, the considerable lapse of time involved (except under gas anesthesia) justifies the elective low forceps operation. The application of forceps in the mid-pelvic levels, on the other hand, involves a certain risk to the fetus which increases rapidly with the height of the head. Mid forceps, therefore, is not justifiable unless the risk to the fetus is less from the forceps than from permitting the head to remain in situ. The six principles enumerated in the first part of this discussion must always be kept firmly in mind and rigidly observed.

(*a*) Simple arrest of the head in an occipito-anterior position. This is usually due to one of two things: incomplete dilation of the cervix, or insufficient moulding in cases of cephalopelvic disproportion of either type (large head or small pelvis). In a few cases the arrest may be due to contraction or deformity of the middle and lower pelvis. It is obvious, in either case, that the decision in favor of application of the forceps should not be made hastily. Extreme care should be taken to be certain that the cervix is really completely dilated; if it is not, more time is required. If the head is arrested solely through disproportion or moderate extension, time again affords the only safe means of adaptation of the head to the pelvis. Time is the most valuable instrument in the obstetrician's armamentarium. I once heard the late Dr. Ross McPherson say: "Gentlemen, have you ever noticed the ease with which the consulting obstetrician delivers the difficult case?"—meaning that the time which has been required to bring the consultant to the bedside has permitted the natural

forces to convert the difficult into an easy case. In such situations it is generally best to wait half an hour after the decision to apply the forceps has been made.

(*b*) Persistent occipitoposterior positions and transverse arrest. In these situations we have not only a disproportion of adaptation, but an increase in dystocia on account of the tendency of the head to extend. It is difficult to define exactly the term "persistent." Probably in about half of all cases the head enters the pelvis in the transverse or posterior position, and natural adaptation brings the head into the anterior position in the mid-pelvic levels in all except a small percentage of cases. It is better to permit this process to occur, because there is less trauma to the head and to the maternal soft parts, and because no element of potential infection is introduced. As long as there is no undue extension, and the head fits loosely in the pelvis, forceps should not be employed. On the other hand, increasing extension or impaction create a situation which cannot be solved by nature without a marked risk of intracranial damage, and early use of the forceps is indicated. In rather rare cases, trachelotomy (Dührssen's incisions) may be necessary to the favorable outcome of the case.

The introduction and placement of the blades may be difficult, but this does not justify a haphazard application. Much more than in low forceps is the proper application necessary. One may be guided to some extent by fixed rules, but in numerous instances the orthodox rules must be abandoned and a technique adapted to the case invented. My own rule in such cases is to apply "the more difficult blade" first, since the absence of the other blade gives more room for maneuvering the first. Having the buttocks an inch or two beyond the end of the table facilitates greatly the application of the anterior blade; in rare instances a preliminary episiotomy makes a great deal of difference. The first blade should be placed as accurately as possible, although it is almost certain to be dislodged to some extent during the introduction of the second blade. When both blades are in place, their accurate placement in relation to the head should be effected; whereupon the problem (often difficult) of accurate locking frequently arises. The blades should be manipulated in and out with the greatest gentleness and with the mental eye fixed upon the tips of the blades with regard to the various curves of the forceps, the head, and the available cephalopelvic spaces. After locking has been effected, the cephalic application must again be checked and corrected if necessary.

In rare instances it may be necessary to employ the Kielland type of forceps. If any of the standard types of forceps is employed in cases of transverse arrest, a normal application should be made so that reapplication after rotation will not be necessary. In posterior positions, of course, a reverse application must be made, with reapplication after rotation.

The rotation is best effected by Bill's modification of the Scanzoni maneuver: the handles must be deflected in the direction of the sinciput (for the sake of whatever flexion is possible) until the long axis of the *blades* coincides with the axis of the pelvis; the tips of the handles are then swung in a circle of a radius sufficient to keep the axes of the blades and of the pelvis coincidental. It is a good plan, if possible, to overcorrect slightly (the sagittal suture being rotated a little past the sagittal plane of the pelvis) and to have an assistant grasp the body of the fetus from above in order to lessen the tendency to backward rotation as the blades are removed. I find it much simpler to employ two pairs of forceps, and to apply the first blade of the second forceps before removing the second blade of the first forceps (Tucker-McLain for rotation, Elliott for extraction). Of course, if the Kielland forceps is used, reapplication is generally unnecessary. Traction must be made along the axis of the birth canal, backward and downward, merging with progress into downward until the outlet is

reached, when the traction of low forceps is employed.

3. The use of *forceps on the aftercoming head* in breech presentations is one of the most life-saving procedures in obstetrics. Relieving, as it does, the strain on the cervical spine and the great nerve plexuses, it also affords a means of steering and flexing the head and an opportunity of providing an airway to the nose and mouth of the fetus which may be utilized when the extraction of the head must be made slowly in order to avoid the intracranial damage incident to excessive pressure and rapid moulding. Episiotomy is almost essential, although where the perineum is apparently elastic enough, episiotomy may be deferred until the need for it becomes apparent. For the obstetrician working without an assistant, especially in the home, it is probably best to perform a preliminary episiotomy. Before applying the forceps the patient should be brought down until the buttocks project at least 2 inches over the edge of the table or bed because, since the procedure is essentially a high forceps, the initial traction must be made directly backward. As soon as the arms are delivered, and before any traction comes upon the head, two fingers should be introduced under the fetus to the lower part of the face: whereupon gentle manipulation will flex the head into the most favorable attitude and steer the chin into the more convenient posterior oblique diameter of the inlet. If the head is jammed in the inlet it may be dislodged by pushing the body of the fetus upward. Flexion and position must be maintained by the fingers while the blades are applied with the other hand.

The orthodox application is made from beneath the body of the fetus, which is held forward and out of the way by an assistant. (Care should be taken to avoid hyperextension of the neck, which may cause serious injury.) When working alone, the obstetrician will find it much easier to apply the forceps over the shoulders of the fetus from behind its back, the body being allowed practically to dangle vertically. In some cases this application will be found to be much easier than the orthodox one, since the tips of the blades can be introduced immediately along the base of the skull on each side, and allowed to follow the contour of the head under direct visual inspection. After checking the application, traction should be made in the axis of the superior strait, i.e., almost directly backward (toward the floor). If disproportion offers an obstacle, an airway to the fetus may be provided between two fingers or, better, by introducing a Sims speculum along the posterior wall of the vagina and wiping or sucking the fluids away from the nose and mouth. Provision of an airway permits one to take as much time as is necessary for safe moulding of the head. As the head descends, the direction of traction is of course altered to follow the axis of the birth canal.

There is a final point which requires a brief discussion, that is, whether signs of distress in the fetus, as evidenced by rapid, slow, or irregular heart action, should be considered as an indication for immediate delivery. It must be remembered that fetal distress of this type is evidence of either shock or intracranial pressure and that rapid delivery is apt to increase greatly and abruptly the underlying causes of the pathologic status. In other words, rapid delivery may determine a fatal issue which might have been avoided by leaving the forces of nature to their gentler and slower solution of the problem. This is especially true in cases where the fetal distress is brought about by excessively powerful uterine contractions or bearing-down efforts on the part of the mother. In such cases slowing of the labor by anesthesia is the only reasonable treatment. If the distress becomes manifest in the low position, episiotomy and forceps (if necessary) constitute the best solution. If the head is at a level higher than midpelvis, if the cervix is incompletely dilated, or if disproportion exists, it is better not to employ the forceps. Malposition of the

head should be corrected, using the forceps if necessary; but it is frequently best, in such cases, not to employ the forceps for traction, until the condition of the fetus has markedly improved. It is in the mid-pelvis that the greatest care and judgment in regard to the employment of the forceps become essential. If in doubt, leave the situation alone.

CONCLUSION

The obstetric forceps properly used is one of the most valuable of all instruments; improperly used it may be productive of disaster. The foregoing discussion is an attempt to summarize the principles and rules which help to eliminate the risk involved in the improper use of this instrument.

WOMEN, for one cause or another, and there are many, may become so accustomed to a leukorrhea—a discharge from the uterus or vagina—that they altogether ignore the suggestively odorous, pinkish discharge of early cervical cancer.
From—"A Textbook of Surgery" by John Homans (Thomas).

INJURIES AND REPAIRS OF THE BIRTH CANAL DURING LABOR

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IN the practice of obstetrics, the commonest abnormality with which we have to deal is laceration of the structures of the parturient canal. The usual and most accepted classification of these lacerations is in the two devisions of perineal and cervical.

The perineal lacerations are divided into three types: first degree—lacerations of the mucous membrane of the vaginal canal only; second degree—including lacerations of the muscle structures of the perineal body and rectal sphincter; third degree—or complete lacerations which involve the rectovaginal septum to the degree of entering the lumen of the rectum.

It is an understood fact in obstetric teaching today, that if nature were permitted spontaneously to deliver a primiparous mother of a single child, in the vast majority of cases, one of the three types of laceration would result. However, these lacerations may occur even after every precaution has been taken, and it is only necessary to examine the birth canal of a multiparous patient to realize that serious damage may be done to the supporting structures with resultant relaxation and formation of rectocele and cystocele.

Lacerations of the posterior vaginal canal are more common than anterior ones. The integument may not necessarily be affected, as frequently the supporting structures, particularly the fascia, relax sufficiently during the passage of the child through the birth canal, so that the mucous membrane of the vagina escapes injury. Anatomically, the anterior portion of the vagina is much shorter than the posterior portion and is less likely to become injured, if the cervix is allowed to become fully dilated and effaced before any operative procedure is attempted.

The mechanism of labor in breech as well as vertex presentation consists of rotation, flexion, molding and descent, all of which are essential in guiding the passenger's approach towards the vaginal outlet.

All lacerated areas, even those of minor or first degree type, are potentially infected by the normal vaginal flora which may become pathogenic in traumatized and devitalized tissue. The possibility of infection increases materially with the extent of the injury. Lacerations may be single or multiple, and may occur in the anterior, lateral, or posterior walls. However, operative delivery and intervention, if not attended with every precaution, are very prone to increase the number and severity of these lacerations. There are some obstetricians who are firm believers in operative delivery, as they feel better able to prevent injuries to the birth canal when the passenger can be instrumentally guided and controlled.

Injury of the birth canal is particularly associated with primigravidae, and one of the best preventive measures is the allotment of adequate time to permit these structures gradually to relax and not be forcibly overstretched, lacerated, or torn by too hasty a delivery procedure. As we consider the perineal body, the transversus perinei, and levator sphincter ani to be the supporting structures, it should be our aim to prevent injury of these parts whenever possible.

In recent years we have learned that it is a safer and wiser procedure to incise or cut into the perineal body, rather than permit it to be lacerated voluntarily. This incision is

termed "episiotomy." When this procedure is followed, the tissue can then be repaired primarily and widespread trauma avoided. It is a well recognized fact that traumatized tissue is a fertile field for local infection and that a more satisfactory result is obtained if tissues, muscle, fascia, and vaginal mucous membrane are untraumatized. Episiotomy has met with such good results that it is now almost routine in every well regulated maternity hospital where sufficient well trained and competent physicians are present to perform outlet forceps operation, prophylactic forceps, or breech extraction, and to properly repair episiotomy upon completion of delivery.

All lacerations of the birth canal should be subjected to primary repair, which means immediately following delivery of the child, if the patient's condition warrants a short continuation of an anesthetic, which is necessary to accomplish this procedure. This applies to the more extensive injury of rectovaginal septum and complete lacerations involving the sphincter muscle and lumen of the bowel, as well as minor lacerations.

Prevention is the keynote of success and it is in the interest of the birth canal structures that episiotomy with forceps extraction of the vertex, or episiotomy with breech extraction, is advised in all primiparous patients and many multiparous individuals.

Injuries to the clitoris and urethra are occasionally met and the bleeding associated with these is often excessive in amount. All bleeding points in the vaginal area should be noted and controlled. This may be done by suture or ligation. It should be distinctly understood that it is imperative for the operator performing the repair to return the structures to their original anatomic position. There seem to be several very erroneous ideas prevalent, relative to repair of vaginal injury. In episiotomies as well as in spontaneous lacerations of any degree, repair must be undertaken with several important facts in mind, namely, unsatisfactory results are usually due to (1) improper technique in preparation of patient; (2) poor apposition of the structures; (3) too heavy or too much suture material, whether absorbable or nonabsorbable; (4) too securely knotted sutures which restrict drainage as well as circulation.

Primary union should be our aim and primary repair should be instituted whenever possible. It is truly remarkable, however, that fairly satisfactory, and occasionally very satisfactory, results may be obtained even though poor apposition and incompetent surgical technique have been used. This method and the method of allowing the structures to approximate themselves without repair, are not advocated.

After-care of perineal lacerations is equally important in accomplishing good results. All suture material and the areas about the vaginal canal should be scrupulously cleansed, dried and protected at frequent intervals. If evidence of infection is manifested by edema, redness and tenderness, application of a hot, wet, surgical dressing is preferable to removal of the sutures.

Absorbable perineal sutures are advocated in the repair of these lacerations in most instances. It has been proved that silver wire, silk, linen, and silkworm gut, have a tendency to cut through tissue because of their inability to yield to the structural and histologic changes in the healing process. Absorbable sutures are more satisfactory because of their elasticity and flexibility.

It is very important that lacerations of the birth canal must not be approximated too tightly, as in all these tissues during the process of healing there is serum present and lochial materials flowing over both the mucous membrane and integument surfaces. A wound that is sealed too tightly, as is the practice followed by some in using a subcuticular perineal stitch, is very likely to collect pockets of secretion which may eventually become infected and result in local inflammatory reaction. One of the most eminent obstetricians in the country

has stated, and it is a good thought to remember, that if all sutures were tied over a hemostat, better and more satisfactory results would be obtained.

The end-results of repair of the birth canal should include complete restoration of the sphincter and bowel control, in the third degree lacerations; a supporting and flexible perineal muscle sling in the second degree lacerations; and an even and smooth union of the vaginal mucosa in those of minor or first degree.

Primary repair is advocated, if possible. However, if a patient's condition does not warrant repair immediately following delivery, intermediate repair should be carried out, at which time the same general principles should be followed as in doing primary repair. Five to seven days postpartum seems a sufficient length of time between delivery and intermediate repair. If at the end of this time intermediate repair is contraindicated, secondary repair may be done following the termination of the puerperal state. It is wise not to postpone secondary repair too long, particularly in third degree lacerations, as retraction of the sphincter within its sheath often causes some difficulty in its proper apposition and adjustment. The rectal wall is likewise more difficult to approximate and the formation of scar tissue tends to poor healing and union and increases the possibility of a breakdown of the repaired structures.

In rectovaginal fistulae and complete tears of the perineum, it is often wise to proceed with severance of the sphincter muscle by incision in its posterior portion, in order better to approximate the retracting ends. This seems to relieve a great deal of discomfort and pain. Particular attention must be paid to the residual material collecting in the rectum above the sphincter repair.

In postoperative care and treatment, the diet is of importance. Liquid and non-bulky diets should be adhered to. Liquids should be given for the first three or four days and proper enema and postoperative bowel technique, such as rectal instillations of oil, as well as oral administration, should be carried out to obtain the best results. Sphincter control is brought about occasionally by formation of scar tissue, but in most instances this cannot be considered a satisfactory result.

Repairs of the urethra should be accomplished as a primary operation and satisfactory results may be obtained if an indwelling catheter is placed in the bladder for from three to five days.

Vesicovaginal fistulae and vesical lacerations should be immediately repaired. Indwelling catheters and proper irrigation of the bladder should be instituted for one week postpartum. Particular attention is directed towards the free escape of bladder fluid through the catheter, which is necessary in order to avoid distention of the bladder before primary union has taken place. This usually occurs one week to ten days postoperatively.

All external lacerations such as lacerations of the labia minora, labia majora, and episiotomies, whether they be median, mediolateral, or lateral, can be accomplished as described in repair of the primary lacerations of the birth canal.

The cervical lacerations vary in number and extent and may be unilateral, bilateral, single or multiple. There is seldom, if ever, a birth through a nulliparous cervix which does not destroy some of the continuity of the cervical structures, either the external or internal os, or cervical canal. Small cracks or nicks in the cervical mucosa which do not cause profuse bleeding can be demonstrated in almost every puerperal cervix. Primary lacerations can be prevented to a great extent by allowing sufficient time for the cervical canal to become effaced and the cervical os completely dilated. Forceful dilation is in error except where indications point to a dystocia of the cervix or where it is necessary to dilate the cervix rapidly in the interest of either mother or child. Accouchement forcé, forceful dilatation of the cervix and extraction of the child, is responsible

for very damaging injury to the pelvic structures.

The accepted classification of cervical injuries is: first degree or primary lacerations—small endometrial or mucous membrane tears; second degree—lacerations in the cervical canal up to the internal os, unilateral, bilateral, or stellate in type; third degree—lacerations which enter through the internal os and extend up to the fornices of the pelvis and very often into the lower portion of the broad ligament.

It is not always advisable to suture the primary lacerations if they are not bleeding at the time of inspection of the cervix. Prevention of these injuries is necessary at all times. No operative procedure through an undilated and uneffaced cervix is ever justified. Forceps delivery through an undilated cervix is not only dangerous but is considered very poor technique. Dilatation of the cervix and internal podalic version may be accomplished without severe injury to the cervix if sufficient time is allowed for gradual and complete manual dilatation. Great damage is done when manual dilatation is not completed before internal podalic version is attempted. Artificial delivery with partial dilatation is usually the cause of the extensive lacerations of the cervix which fall under the third degree type. Extensive hemorrhage occurs and extension of the laceration may enter the pelvic portion of the abdominal cavity as well as the corpus of the uterus.

Following all procedures, such as manual rotation of the vertex, internal podalic version or Braxton Hicks' version, or forceps delivery in transverse arrest of the head and posterior positions, the cervix should be inspected. In every instance where the uterine cavity has been invaded to facilitate delivery, as in abnormal positions, transverse arrest, and breech extractions, inspection of the cervix and immediate repair of lacerations present is advisable.

The same principles apply in the repair of lacerations of the cervix as in lacerations of the perineum. Hemostasis as well as approximation of the tissue is the primary aim. As the hemorrhage is often excessive, deep and full sutures are occasionally required, tightening the sutures only sufficiently to approximate the structures and control the hemorrhage.

Inspection of the cervix is at times a rather difficult procedure and therefore every delivery room table set-up should be equipped with the proper specula for viewing cervical areas and proper sponge forceps to be used as a tenaculum. The cervical tissues are soft, friable, often edematous, even at times hemorrhagic, and severe injury can be done by tearing cervical structures with the tenaculum. Retraction of the vaginal canal with the proper speculum makes the drawing down, inspection, and suturing of the cervix a simpler procedure. It is very distressing to inspect the cervix after delivery and try to realize that this seemingly badly traumatized cervical area could ever regain its normal appearance. It is truly marvelous to discover upon inspection several weeks postpartum that what seemed at the time of delivery to be a hopeless condition healed through the process of involution and actually is again a satisfactory structure.

Routine inspection of the cervix is not advised unless the bleeding is characteristic of cervical injury or unless some of the operative procedures heretofore mentioned have occurred. Cervical injury can usually be readily diagnosed and can be differentiated from perineal laceration bleeding which is usually dark in color and of more venous character and generally easily visible. Cervical bleeding is definitely arterial in character and there is a constant trickle from the birth canal while the uterus is well contracted. This is in contradistinction to the bleeding from the uterine cavity which is associated with a soft, non-contracting uterus, when the bleeding occurs in gushes through the vaginal orifice.

Intermediate repair of the cervix may be accomplished when necessary during the puerperal state. Secondary operations on

the cervix, or trachelorrhaphy, are not under discussion here.

Frequently extensive lacerations of the cervix extend into the corpus of the uterus. This is accompanied by bleeding into the abdominal cavity and may, if not too extensive, he repaired from the vaginal area. If, however, these lacerations are above the internal os, directly behind the bladder, posteriorly, or in the broad ligament, it is necessary occasionally that they be approached from the abdominal route.

Diagnosis of uterine rupture can be made by palpation from below. Upon examination the hand passes through the uterine wall directly into the abdominal cavity. Supravaginal hysterectomy is usually necessary and all facilities must be at hand and be utilized to replenish blood loss and to combat surgical shock. Vaginal packing and uterine packing may in certain instances temporarily stop the flow of blood from the laceration until the patient can be properly prepared for abdominal laparotomy.

Spontaneous rupture of the uterus has been occasionally reported. Usually there is an etiologic factor of previous endometritis or infection, intramural fibroids, previous operation such as myomectomy, cesarean section, or suspension operation. Particularly must we consider those operative procedures where the convalescence has been febrile and the postoperative course stormy. Reports of spontaneous uterine rupture seem to occur more frequently in those individuals who have had previous cesarean section performed because of cephalopelvic disproportion.

Ruptures of the uterus are classified as complete and incomplete. Some ruptures occur easily in labor while others are the result of protracted and prolonged labors, as well as operative intervention at the time of delivery.

Since Baudelocque, Bandl and many other early investigators gave us a more elucidated picture of this condition and called our attention to the anatomic structures of the uterus, especially the lower segment, the handling of uterine rupture has been a controversial subject. Today the pendulum is swinging towards cesarean section in the lower segment of the uterus, as the procedure of choice. This brings to mind the controversy of thirty or forty years ago when the lower uterine segment of the parturient canal was brought under closer scrutiny. The older authorities maintained that rupture was more apt to occur during labor, in the lower segment which was the stretchable and dilatable portion, than in the upper portion of the uterus where the musculature contracted. Their supposition was that this contractile portion might prevent the uterus from rupturing. The fundal cesarean section, whether in emergency or electively performed, afforded in their opinion a safer area for healing than would the lower cervical portion of the uterus. Whether the incision was longitudinal or vertical, made little or no difference, but unquestionably the low cesarean section in potentially and infected cases, has reduced the maternal mortality to such an extent that the low operation is now justifiable in these cases.

The extraperitoneal operation as well as the classical type of cesarean section is subject to the accident of rupture in subsequent labors, particularly is this so when abnormal presentations and positions and relatively all absolutely contracted pelves, exert an excessive amount of contractile action on the uterus. Occasionally partial ruptures have been reported where the muscle had separated while the peritoneal covering of the uterus remained intact. Lacerations may be in any portion of the uterine corpus, but complete rupture includes the entire uterine structure. Most ruptures seem to occur in the lateral and transverse areas in the supravaginal region.

The prevention of rupture of the uterus is the keynote of success in individuals whose etiologic factor may be the causative factor. All individuals who have a relatively contracted pelvis must be considered at least potential subjects for repeated or second operations of cesarean section.

When threatened partial or complete rupture of the uterus occurs the patient gives a very definite symptomatology and clinical picture. Uterine contractions cease, constant abdominal pain replaces intermittent uterine contractions, blood pressure falls, pulse rises rapidly, and there is a tender local area. All of these symptoms are forerunners of oncoming rupture followed by surgical shock. Profuse vaginal bleeding may occur through the cervix or massive hemorrhage may occur in the abdominal cavity.

Prompt surgical intervention is imperative. Previous to the onset of an operative procedure to relieve this condition, the general condition of the patient must be immediately considered. Blood transfusions and intravenous fluids are necessary. Operation should not be performed while the patient is in profound surgical shock. It has been reported that the placental structure and fetus have been found in the abdominal cavity extruding through the rent in the uterus and the uterus in contraction when the abdominal cavity was opened. Hysterectomy with immediate control of hemorrhage is advisable in most instances. In a partially ruptured uterus the contents of the uterus may be evacuated and the repair of the rupture performed. Some authorities advocate porro cesarean section in partially ruptured uterus or in suspected ruptured uteri. The elective method and decision as to the most advantageous time for operation has been demonstrated repeatedly by the low maternal and fetal mortality. The high maternal and fetal mortality is attributed to those individuals who have had loss of blood, a prolonged labor, and an emergency cesarean section.

If partial rupture of the uterus occurs during dilatation of the lower uterine segment, it is usually confined to that portion of the lower segment and after delivery is accomplished from below through the birth canal, proper tamponade and packing of the uterus may be sufficient to control hemorrhage. At times temporary methods may be used which allow a more favorable condition to become present in the individual so that blood loss and surgical shock may be combated or prevented before operative procedure is instituted.

The contraction of the uterus between the upper portion and the cervical segment at the area of Bandl's ring, has been responsible for many ruptures of the uterus. When, however, a complete rupture has occurred and the laceration extends into the peritoneal cavity drastic and prompt operation has met with rather unusual success.

As the placenta is usually situated over the old previous scar tissue and there is infiltration of the chorionic villi into the decidual layer of this region, this may be an important factor in the rupture of the uterus after a previous cesarean section.

Prolonged second stage of labor with sudden cessation of uterine contractions and constant lower abdominal pain and tetanic condition of the uterus seems to be indicative of rupture. Bandl's contraction ring can usually be palpated without difficulty and is usually present at or below the umbilical area.

The uterus may be traumatically ruptured during operative procedures, as in internal podalic version, in cases of undiagnosed monstrosities, and hydrocephalic infants, where pressure from the intrauterine fetal structures has caused a necrosis of the uterine wall. Occasionally the fetal structure which has been expelled from the uterus into the abdominal cavity can be clearly felt by abdominal palpation.

Prognosis in complete and incomplete rupture of the uterus is far more favorable now than it was previously, as prevention and prophylaxis against rupture are more clearly understood. We consider uterine rupture which occurs in an individual with the possibility of a suspected rupture, a preventable accident. A careful history will often outline the possibility of rupture.

Previous pregnancies, miscarriages, operations, repeated abortions and curettage, all must be considered in the prophylactic care.

If rupture should occur when the passenger is low in the birth canal, extraction by forceps may occasionally be indicated but should not be undertaken until immediate operative preparation is accomplished.

In the partial and complete ruptures of the uterus many methods of treatment are advocated. Some authorities feel that all incomplete ruptures should be packed while others advocate porro hysterectomy. Some feel that hysterectomy and panhysterectomy should be carried out in all cases of complete rupture. No specific operation can be devised as each case must be individualized.

Maternal mortality in most ruptures of the uterus is attributable to hemorrhage, shock, or sepsis. In the accident of uterine rupture, be it complete or incomplete, premonitory symptoms and etiologic factors are always present and play a most important part in determining the ultimate result. Definitely the prognosis is better if the interval between rupture and operation is of short duration. The less loss of blood, the more favorable the prognosis; the shorter the labor, the better the prognosis; and all immediate treatment at our command must be instituted to prevent accompanying shock.

The ovary is particularly subject to cyst and tumor formation, a process which is sometimes purely one of retention of fluid and sometimes a combination of retention with actual new growth.
From—"A Textbook of Surgery" by John Homans (Thomas).

POSTPARTUM HEMORRHAGE*

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POSTPARTUM hemorrhage is still a major factor in maternal mortality in this country. Although there has been a progressive and an appreciable decrease in maternal deaths during the past five years, deaths from hemorrhage have been little affected, averaging 6 to 6.5 per 10,000 live births. Proportionately, hemorrhage looms as an ever increasing cause of death among the three major causes. These statistics do not tell the entire story, for hemorrhage is often an important contributory factor in the development of puerperal infection. Stander has noted that the incidence of infection in all hospital deliveries is 11.2 per cent, whereas this incidence increases to 27.2 per cent following postpartum hemorrhage. It must, therefore, be noted that some of the puerperal deaths attributed to sepsis must be charged indirectly to hemorrhage. Still another interesting phase of this problem is the fact that serious postpartum hemorrhages are largely preventable and mortality can be eliminated almost entirely. This has been possible in the larger centers and should be possible in general practice.

Bleeding during the third stage of labor has too long been regarded as a normal accompaniment of parturition. Physicians have been taught that pregnancy fortifies the patient against an excessive blood loss by an increased blood volume. Dieckmann and Wegner and a host of other investigators have pointed out the fact that this increased blood volume is largely the result of a blood dilution, so that the cellular and hemoglobin content per unit volume of blood is actually less at the time of labor than at the onset of pregnancy. The vital blood constituents in a serious hemorrhage are the blood cells and their oxygen carrying hemoglobin. Thus, this apparent safeguard against excessive bleeding is in reality a deception. During the first part of pregnancy there usually occurs a diminution in blood volume and blood constituents, often resulting in a real anemia. Should labor intervene at this period and be accompanied by a serious blood loss, the hazards of excessive bleeding would be increased.

Thus, in the prophylaxis of puerperal hemorrhage, accurate knowledge of the blood state is essential. Every pregnant woman must have a blood examination to determine early in the prenatal period the hemoglobin and cellular content and again, ideally, just before labor. This is as essential a procedure as the now accepted routine tests for the presence of syphilis. If an anemia is present, the patient should be placed on suitable therapy. It may even be necessary to resort to blood transfusions in marked anemias discovered late in pregnancy. Present day practice emphasizes prevention rather than cure and in no other field is this principle so important as in obstetrics.

There can be no sharp line between a normal and an abnormal blood loss. Although the average blood loss during the third stage of labor is approximately 300 c.c., wide variations occur. Usually a blood loss of over 500 c.c. is considered pathologic and is classified as a postpartum hemorrhage. The amount of blood loss which will provoke symptoms in one patient may produce little change in another. The size of the individual, the state of her blood,

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her physical condition, particularly the presence of dehydration, all influence the hazards of an unusual blood loss. Pastore suggested that the blood loss be estimated in relation to the body weight and thus, indirectly, to the blood volume. A blood loss of more than 1 per cent of the body weight would comprise a postpartum hemorrhage: i.e., 600 c.c. in the patient who weighs 60 Kg. The determination of hemoglobin and cell volume provides an even more accurate evaluation of the blood loss. These measures may not be possible in the general practice of obstetrics, but they do emphasize the importance of an accurate measurement of the blood lost at the time of delivery and the importance of maintaining this blood loss at a minimum.

INCIDENCE

The frequency of postpartum hemorrhage varies considerably. It occurs less often in women who are delivered naturally, with little or no analgesia or anesthesia. Tucker and Benaron reported an incidence of 4.2 per cent in the home delivery service of the Maternity Center where 79 per cent of the deliveries are conducted without pain-relieving drugs of any kind. In contrast to these figures Peckham and Kuder reported an incidence of 6.14 per cent at the Johns Hopkins Hospital and Pastore 6.4 per cent at the New York Lying-in Hospital.

Many factors influence the likelihood of abnormal postpartum bleeding. Analgesia and anesthesia increase the hazards of the third stage by their effect on uterine tone and motility. Deep anesthesia may cause marked uterine relaxation, interfering with the normal mechanism for the control of bleeding in the third stage. The almost routine use of sedatives and anesthesia in hospital practice necessitates the use of oxytocic drugs to combat their effects during the third stage of labor. Overdistention of the uterus may increase the postpartum blood loss. This excessive distention may be due to an excessively large baby, a multiple pregnancy, or an abnormal accumulation of liquor amnii. There is a definite relationship between the length of labor and the frequency of postpartum hemorrhage. Pathologically long labors increase the incidence of abnormal bleeding. Unusual operative interventions such as version and extraction, difficult forceps delivery, or operations on the cervix tend to increase the blood loss. Special precautions should be taken in any of these conditions in which there is a tendency to an abnormal blood loss so as to decrease the danger of hemorrhage.

Improper conduct of the third stage of labor is the most common cause of an unusual blood loss during this period. The failure to recognize complete placental separation may lead to premature attempts at the expulsion of the placenta with a greatly increased blood loss. Delay in the expression of the placenta from the lower uterine segment may result in continued bleeding behind it. Unintelligent manipulation of the uterus during the third stage of labor increases the incidence of a pathologic third stage and its concomitant increased loss of blood.

THE THIRD STAGE OF LABOR

The proper appreciation of the mechanism and conduct of the third stage of labor is essential in the prevention of an abnormal blood loss. Recent contributions have clarified our understanding of this important phase of parturition. The proper conduct of the third stage must take into consideration its mechanism.

The placenta remains firmly attached to the uterine wall during the first and second stages of labor. The surface area of the placental site is approximately that of the placenta. (Fig. 1.) On the evacuation of the uterus, the uterine cavity is greatly reduced in size. This reduction is the result of contraction of the uterine wall so that it increases several times in thickness. This sudden decrease in the size of the uterine cavity results in a concomitant reduction of the surface area of the placental site. (Fig. 2.) This reduction takes place equally,

by a shrinking of the entire area rather than by a closing in of the periphery of this area. The placenta is a rather rigid organ

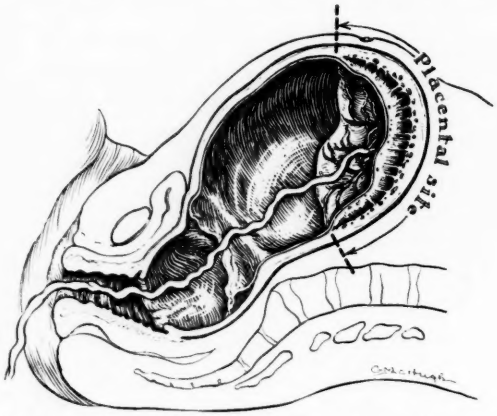

Fig. 1. Shows the normal uteroplacental relationships when the cavity of the uterus is distended with the fetus. Note the length of the placental site indicative of its surface area and the characteristic discoid shape to the uterus.

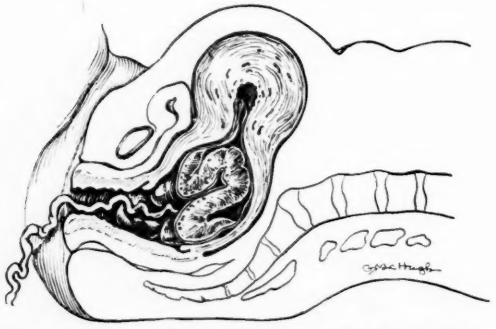

Fig. 3. Shows the uteroplacental relationships after the expulsion of the placenta into the lower segment and vagina. The fundus of the uterus has become globular and has risen; the lower segment is distended by separated placenta.

and does not contract with a diminution in its site of uterine attachment. This physical change must result in a shearing off or separation of the placenta in its vulnerable plane, the spongy decidua basalis. The more perfect this mechanism functions the more completely the placental separation will take place. The retroplacental clot is not necessary in the mechanism of separation. In most instances it accumulates as a result of an incomplete placental separation or after the placenta has separated from its attachment, while its expression from the lower uterine segment and vagina has been delayed. The time consumed by the third stage is largely due to the phase of expulsion, for the phase of separation is completed very rapidly.

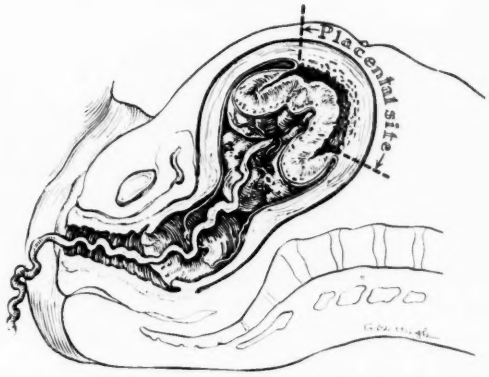

Fig. 2. Shows the uteroplacental relationships immediately after the baby has been expelled from the uterus and the placenta has separated from its uterine attachment. Note the great decrease in surface area of the placental site, the thickened uterine wall and the change in uterine contours.

The ideal conduct of the third stage consists of the recognition of placental separation and the immediate expression of the placenta after separation has taken place. The most reliable sign of placental separation is the change in the shape and position of the uterus. Immediately after delivery the organ can be palpated as a softened, discoid, pear-shaped body, the top of which reaches below the umbilicus. Immediately after separation of the placenta, the globular contracted corpus can be palpated at the level of the umbilicus, the softened lower uterine segment distended by the separated placenta above the symphysis. (Fig. 3.) The rise of the uterus in the abdomen is the result of the placenta being pushed out of the corpus and into the lower segment. Other signs of separation can be noted, but they are less valuable. The cord outside the vagina advances and a gush of blood may occur at this time.

In the expression of the placenta, several safeguards must be exercised. The corpus must be in a contracted state before expression begins. The entire uterus must not be pushed downward into the pelvis because this dislodgement favors excessive bleeding. The venous return is shut off and

the uterine sinuses become overfilled with blood, thereby tending to increase the blood loss. Pastore has suggested a method to prevent this undesirable complication, but the method is not applicable when the attendant is conducting the labor without help. The left hand is placed flat on the abdomen with the fingers directed under the symphysis, thereby preventing the uterus from entering the pelvis while the right hand expresses the placenta. The same end can be accomplished by the accoucheur if he will make pressure with the fingers of the left hand just above the symphysis while the right hand pushes down on the corpus. When the placenta is visible at the introitus, slight traction on the cord will deliver it most easily. However, traction on the cord is to be seriously condemned, for such manipulation on an incarcerated or partially adherent placenta may result in inversion of the uterus.

An oxytocic drug should be administered immediately after the expulsion of the placenta. Ergonovine 0.2 mg. intramuscularly is the most effective drug because of its prolonged action. In the service of the Chicago Lying-in Hospital it has almost entirely replaced pituitary preparations. Pituitary extract or its oxytocic fraction, pictocin, can be given, but the action of this drug is so short that ergonovine should be given orally to maintain uterine tone.

Hospital practice with its increased use of analgesia, anesthesia, and the artificial termination of pregnancy has resulted in a change in the conduct of the third stage. In many institutions patients receive 1 c.c. of pituitary extract intramuscularly immediately on the birth of the baby. When the drug is administered by this route it probably does not act for at least six or seven minutes so that the phase of placental separation is not interfered with. The contraction of the uterus induced by the oxytocic drug produces a most favorable condition for the second phase, that of expression. The placenta can easily be expressed from the lower uterine segment and vagina, thereby limiting the bleeding following placental separation and decreasing the length of the third stage. Rarely, perhaps one case in a hundred, the placenta becomes incarcerated in a contracted zone between the corpus and lower segment and its manual expression may be difficult or impossible. Should active bleeding take place it may be necessary to remove the placenta manually. This complication is of such rare occurrence that the management of the third stage as described is routine in many institutions. It is not advisable, however, for deliveries in the home.

NEW MANAGEMENT OF THE THIRD STAGE OF LABOR

During the past three years a new management of the third stage of labor has been under careful study at the Chicago Lying-in Hospital. This method has yielded such striking results in the freedom from third stage complications and in the diminution of the blood loss that it is deserving of careful consideration with a view toward its more extensive use. The results in some 5,000 cases and a comparable control series are being carefully analyzed at this time and will be published in the near future.

If the phase of placental separation is entirely a physical phenomenon and is the result of a sudden reduction of surface area of the placental site, then theoretically the more rapidly this reduction takes place, the more complete will be the placental separation. There should be less likelihood of portions of the placenta remaining attached and thus interfering with the third stage. To accomplish this immediate contraction of the uterus following the birth of the baby, 0.2 mg. of ergonovine (ergotrate H, Lilly) is given intravenously after the head is delivered and as the anterior shoulder is brought into view. If one allows twenty to thirty seconds at this point for the drug to exert its action, the baby can then be delivered. The uterus contracts down almost instantaneously, separating the placenta cleanly from its attachment and pushing it out into the lower uterine

segment and vagina. Palpation of the corpus will reveal it to be globular and firm. The placenta can now be expressed from the vagina. This management of the third stage interferes with the phase of separation, whereas an oxytocic drug administered intramuscularly after the baby is born prepares the way for a more favorable phase of expulsion.

The advantages of the method described lie chiefly in the marked reduction in the loss of blood, and the freedom from complications of the third stage and the associated postpartum hemorrhage. The method has proved so effective on our service that the incidence of serious postpartum hemorrhage has become greatly reduced—so much so that the house staff is losing its dexterity in the treatment of this complication. The régime described is only applicable to institutional practice, for it requires someone to give the drug intravenously at the right time. Proper timing in the administration of intravenous ergonovine is essential. There have occurred a few instances of incarceration of the placenta in the contracted zone but this complication is not troublesome in an institution. The method should have a particular appeal in patients who are predisposed to abnormal uterine bleeding by a previous occurrence of postpartum hemorrhage, an excessively distended uterus, a long labor, or difficult operative interventions.

POSTPARTUM HEMORRHAGE

The usual causes of postpartum bleeding are abnormalities of the third stage of labor, uterine atony, and trauma of the reproductive tract. These conditions can be differentiated without difficulty and treatment must be directed to the cause of the hemorrhage. Intelligent management of the patient will do the most in conserving the patient's blood.

Postpartum hemorrhage most frequently results from incomplete separation of the placenta or delay in expression of the completely separated placenta. Premature attempts at placental expression may result in only partial detachment and the typical Duncan mechanism is more likely to separate incompletely. If there is little or no bleeding, no interference is necessary and complete separation should be awaited, careful palpation of the corpus revealing when the placenta has been detached. In hospital practice it is customary to wait as long as an hour in the absence of bleeding. At the end of this time or in the event of frank bleeding, the placenta should be removed from the uterus. Crede's expression should be tried first in an attempt to complete the placental separation and expulsion. The contracted corpus is grasped in such a way that the uterus can be squeezed and pushed downwards at the same time. The uterus must not be pushed forcefully into the pelvis, for this may accentuate rather than diminish the hemorrhage. If moderate attempts at Crede's expression fail to deliver the placenta, manual removal should be employed.

Delay in the expulsion of the separated placenta from the lower uterine segment and vagina will increase the blood loss. The blood accumulates behind the placenta and the clots slowly distend the corpus cavity. This interferes with the uterine contractility, leading to atony and more bleeding. In the proper conduct of the third stage of labor it is important to recognize complete placental separation. While it is inadvisable to interfere with the phase of separation except in case of abnormal bleeding, it is necessary promptly to express the completely separated placenta to maintain the blood loss at a minimum.

Manual removal of the placenta is not an innocuous procedure. Nevertheless, the common feeling is that its dangers have been so well emphasized that the practitioner often delays this procedure at the expense of a serious blood loss. A considerable hazard of infection exists in the invasion of the uterus, but there is even greater danger in delay and continued blood loss. There is a direct relationship between the amount of blood lost and the incidence and severity of subsequent puerperal infection.

Rather than place too great emphasis on the danger of manual removal of the placenta, greater emphasis should be placed on the need of the most scrupulous technique in carrying out this procedure. The accoucheur should cleanse the patient very carefully, draw on a new pair of sterile gloves, and enter the vaginal orifice without contamination. If the placenta is simply incarcerated in the lower uterine segment, it can be removed by grasping it firmly. If a portion of its surface is still attached in the corpus cavity, this part must be separated before the placenta is removed. In the separation of a placenta still attached to the uterine wall, great care should be taken not to traumatize the wall. The entire placenta must be freed before an attempt is made to withdraw it from the uterus. If possible, 0.2 mg. of ergonovine should be given intravenously as the hand is withdrawn. The entire manipulation should be carried out at a single invasion of the reproductive tract. Repeated invasions increase greatly the hazards of infection. It is rarely necessary to resort to uterine tamponade.

Birth trauma as a cause of bleeding can usually be recognized without difficulty. At times, however, a patient may be treated for uterine atony, although this apparent atony is secondary to bleeding from some laceration. The following case is typical of this complication:

A patient was delivered by means of low forceps. The third stage was uneventful except that there occurred a steady trickle of blood during the repair of the episiotomy. The uterus remained firmly contracted. During the following twelve hours the uterus became distended with blood clots on three occasions. The house officer expressed the clots each time by pressure on the fundus and administered an additional oxytocic drug. When the accumulated blood loss became alarming, the patient was carefully examined and blood could be seen spurting from a tear lateral to the clitoris. What had happened was that the blood ran back into the vagina and the uterus. The clots interfered with the normal mechanism to maintain good uterine tone so that the uterus gradually relaxed and became filled with clotted blood. This case history should emphasize the fact that the failure of a good oxytocic drug to maintain uterine tone is significant and a search for other causes of bleeding should be instituted promptly.

Hemorrhage from lacerations and trauma usually manifests itself immediately after the delivery of the baby and before the expulsion of the placenta. It will continue and become more marked after the placenta is out of the vagina. The amount of bleeding will vary with the extent of the trauma. Varicosities that have been cut or torn may cause a sudden profuse and serious blood loss. A small tear in the region of the clitoris can produce a small but long continued blood loss. The slow trickle is more serious than the sudden flooding because the latter excites immediate attention and the flow is stanched while the former may go unrecognized until the total blood loss has become formidable.

Bleeding from an episiotomy incision can be controlled by pressure until the cut tissues can be approximated. Constant pressure should be maintained during the repair because continued bleeding from this source may mount up to an appreciable volume in a short time. Although it is rarely advisable to clamp bleeders in an episiotomy wound, it may become necessary to approximate rapidly the bleeding surfaces before an orderly repair can be undertaken.

Lacerations in the vagina can usually be approximated by interrupted sutures. Ragged, extensive circular tears in the vault may be difficult to visualize. The torn edges should be united as far up as possible and the top suture can be used as a tractor to bring the uppermost portion of the laceration into view. Varicosities of the vagina may be difficult to obliterate. When pressure is removed, the field becomes so flooded that bleeding areas cannot be visualized. It is well to obtain as complete hemostasis as is possible and, if necessary, to resort to a tight vaginal pack. This can

be left in situ for twelve to eighteen hours, after which it can be safely removed. Before placing the pack, one should make certain that all the bleeding is the result of vaginal varicosities and none of the hemorrhage is of uterine origin.

Lacerations of the cervix can usually be brought into view by the use of ring forceps which will not traumatize the cervix. The cut or torn surfaces can be approximated by interrupted chromicized sutures. It is important to obtain good exposure. The uppermost stitch should approximate the very top of the laceration so as to obliterate a torn vessel which can retract into the musculature. The repair should be completed rapidly, for prolonged traction on the uterus may result in uterine venous engorgement and bleeding from this source.

There are certain complications incidental and accidental to pregnancy in which hemorrhage is a major factor. The conduct of the third stage of labor in these conditions deserves special consideration.

Placenta Previa. The placental attachment in the lower uterine segment provides an abnormal mechanism for the third stage of labor. The placental site in this abnormal location does not have sufficient musculature to undergo the same degree of contraction as in the usual location. This lack of musculature interferes with normal contraction and retraction of muscle fibers and bundles and diminishes the value of this mechanism in the constriction of the maternal sinuses of the placental site. (Fig. 4.) Lastly, the lack of a normal decidual buffer zone in the lower uterine wall results in an abnormal placental attachment and an absence of the usual plane of cleavage, further complicating the third stage.

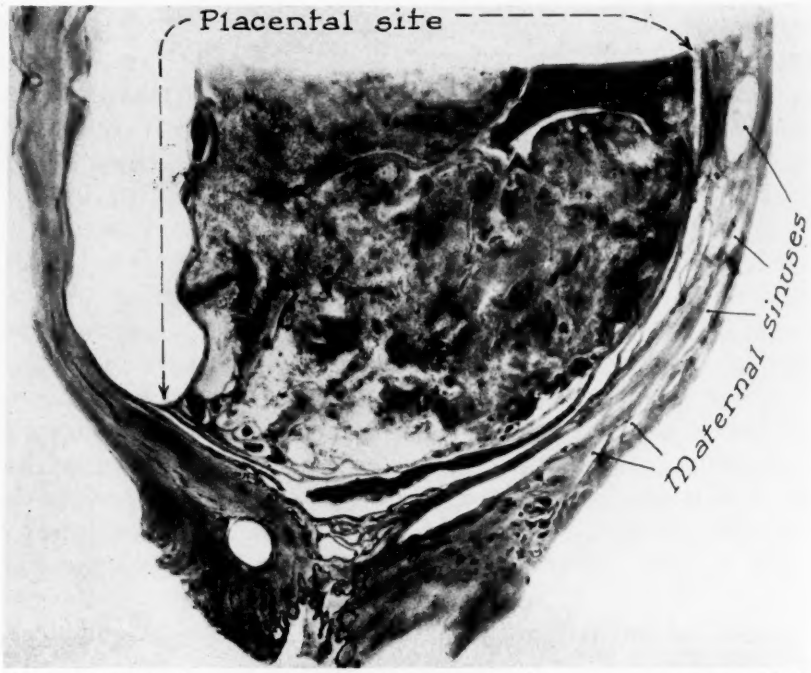

Fig. 4. Histologic preparation of the lower uterine segment and attached placenta in a case of placenta previa. The wall of the lower uterine segment is markedly vascularized by the numerous sinuses of the placental site, thereby altering its normal integrity and making it more vulnerable to trauma. The proximity of the placental site to the cervix increases the hazards of infection.

The third stage may be allowed to proceed normally if there is no abnormal bleeding. As soon as separation of the placenta has taken place, it should be expressed in the manner previously described. The patient should then be given

an oxytocic drug, preferably ergonovine intravenously. If bleeding follows the delivery of the baby, prompt preparation

Fig. 5. This uterus was removed at autopsy from a patient with puerperal infection. Note the retained placental cotyledon in the corpus cavity which first resulted in postpartum hemorrhage from uterine atony and subsequently was the focus of a fatal thrombophlebitis.

should be made for the exploration of the lower uterine segment and the manual removal of the placenta. The placenta must be carefully separated before it is removed. A careful examination of the cervix and lower segment must be made to determine if any trauma has occurred. It must be emphasized that the lower uterine segment in the presence of placental attachment becomes pathologically vascularized and is subject to extensive trauma even with minor manipulations. Any such trauma should be repaired. If bleeding cannot be controlled by suture, it may be necessary to exert pressure against the maternal sinuses in the lower uterine segment by means of tamponade. If only the lower uterine segment is packed, the tampon may serve as a plug concealing bleeding which continues above it. In a rare instance such tamponade may not effectively control the continued hemorrhage in which case preparations for immediate hysterectomy should be made. A rapid operation may save the life of a patient who would otherwise have succumbed.

One final word of caution must be added. Statistics indicate that as many woman die of infection following placenta previa as of the hemorrhage associated with this condition. The close proximity of the uterine sinuses to the vagina and to sources of infection increases the hazards of all manipulations. Extreme care must be exercised in the management of a patient with placenta previa to decrease the hazards of infections.

Abruptio Placentae. Premature detachment of the normally implanted placenta is associated with profuse hemorrhage during the labor and particularly the postpartum period. The hemorrhage may be so overwhelming in amount that the patient is completely exsanguinated within a short time. The control of excessive blood loss in this complication involves the entire management of the condition. The blood may accumulate as a huge retroplacental hematoma, gradually distending the uterus and be almost entirely concealed. Blood may extravasate into the uterine wall between the leaves of the broad ligaments, retroperitoneally, to involve almost the entire pelvis. The separation of the placenta is usually completed or partially completed

at the onset of the accident. The placenta can usually be expressed without difficulty, but the atony of the uterus at this period is the serious problem. A careful removal of all the clots and the intravenous administration of ergonovine should result in good uterine tone providing the uterine myometrium has not been too extensively disorganized by hemorrhagic infiltration. If the uterus fails to maintain good uterine tone, tamponade can be carried out, packing the entire reproductive tract as firmly as possible. Since the advent of the powerful and rapid acting oxytocic agent, ergonovine, we have been impressed with the fact that if bleeding cannot be controlled by this drug, the uterine musculature is probably seriously impaired and hysterectomy should be carried out with all possible speed. Uterine tamponade in these desperate cases only masks the picture and delays the institution of more effective therapy. Timely transfusion of effective amounts of blood is life-saving in these late hemorrhages of pregnancy.

Retained Placental Tissue. In the prophylaxis of postpartum hemorrhage the careful examination of the placenta is most important. This is a responsibility which the accoucheur should not relegate to some other individual. Retained placental fragments or entire cotyledons lead to uterine atony and its concomitant hemorrhage and even more important, they predispose to puerperal infection. (Fig. 5.) If a fragment of placenta is missing, it should be promptly removed. Needless to say, there is danger in the invasion of the puerperal uterus, but with a careful technique, this procedure need not increase the hazards of the patient. The placental tissue can usually be found and peeled off the uterine wall. Membranes left in the uterine cavity rarely cause trouble and are usually passed in the lochial discharges during the first days of the puerperium.

Neoplasms of the Uterus. Fibromyomata of the uterus occasionally complicate the third stage of labor. These tumors may interfere with normal separation of the placenta or with the normal contractility of the myometrium. Although the third stage is usually uneventful, the attendant should anticipate a pathologic third stage and be prepared to meet it. If the placenta fails to separate completely and bleeding intervenes, manual removal may be resorted to. Rarely, a submucous fibroid nodule may cause the abnormal placental attachment. Intravenous oxytocic drugs should maintain good uterine tone, but it may become necessary to tampon the reproductive tract.

Placenta accreta is a very rare complication that may not occur once in 20,000 births. A poor or an absent decidual development results in an invasion of the myometrium by chorionic villi and the absence of the usual plane of cleavage between placenta and uterine wall. This abnormal attachment may involve a small localized portion of the placenta or the greater part of its surface. Manual removal of such an abnormally adherent placenta is impossible. Hysterectomy is the procedure of choice when this condition is recognized.

Inversion of the uterus is a rare complication which results from improper conduct of the third stage. It has not occurred in over 50,000 births at the Chicago Lying-in Hospital. The usual mechanism of production is traction on the cord of the attached placenta when the uterus is in an atonic state. Immediate replacement of the uterus is indicated, following which an oxytocic drug will usually maintain normal relationships. Where the uterus has been inverted for some little time, it usually is necessary to resort to surgical correction. This accident is usually associated with profuse hemorrhage.

Rupture of the uterus may occur during the delivery and produce alarming third-stage bleeding. Immediately after difficult operative interventions a careful exploration of the lower uterine segment and corpus cavity should be made. The rupture can usually be palpated. It may be incomplete and only involve the lower uterine segment in which case repair from below

may be possible. Uterine tamponade may help to control the bleeding more securely. Usually, it is safer to resort to immediate hysterectomy. The operation should be carried sufficiently low so as to include careful ligation of the uterine vessels on both sides.

Rare blood dyscrasias may predispose to excessive bleeding in the third stage. A careful history will usually elicit data concerning the blood deficiency in which event careful blood studies should be made during pregnancy. This is the only condition in which whole blood should be used in any transfusion rather than the usual citrated blood.

PARENTERAL FLUIDS AND BLOOD TRANSFUSION

It cannot be too strongly emphasized that measures for combating blood loss are a most essential part of any treatment of hemorrhage in pregnancy. The subsequent maternal mortality, serious puerperal infection, and prolonged convalescence and invalidism can be greatly reduced by a serious attempt to restore in some measure the blood loss of the patient. For maintaining blood volume, saline or Ringer's solution can be given by hypodermoclysis, using 16 gauge needles. Glucose solution in 20 per cent concentration should be given intravenously at as slow a rate as possible, discontinuing its administration just as soon as blood is available. No more than 500 c.c. should be given unless a liberal blood transfusion follows. It must be remembered that large amounts of hypertonic glucose solution draw liberally on the fluids in the tissues and increase blood coagulation time. Although the blood volume be restored, sufficient circulating hemoglobin must be present to carry on the vital functions of life. The amount of the transfusions should depend on the blood loss, averaging 500 to 800 c.c. in the usual case. Citrated blood is as efficacious as whole blood and can be given easily. Suitable donors must be selected with the greatest care.

The use of acacia as an emergency measure has been advocated. In spite of its appeal because of its ready availability, serious and fatal accidents have been reported. Its use should be entirely discontinued or very guarded.

Blood banks are becoming more numerous so that in time stored blood may be more readily available. At the present time such blood can be obtained only at larger medical centers.

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PUERPERAL INFECTION*

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PUERPERAL infection results when the female generative tract has a lowered resistance to the organisms which invade it during or following delivery or abortion; or when the virulence of the invading organism is unusually great. Of course, both conditions may be present in the same patient. Intrapartum infection is probably much more frequent than is generally believed and can only be prevented by early prophylaxis.

Contamination of the genital tract may be either (1) endogenous, due to organisms harbored by the vagina; or (2) exogenous, due to organisms introduced from without. Prevention of the first type of infection is possible if prophylaxis is started early enough in labor. The latter type of infection must be controlled by preventing the introduction of organisms from without by proper surgical technique—asepsis, antisepsis, proper masking and conservative obstetrical intervention.

A résumé of the findings which have been made since our study of puerperal infection was begun in July, 1924, may be helpful to those who encounter this disease with its various manifestations.

In the report of the Children's Bureau,[1] puerperal septicemia was given as "the most important cause of death connected with pregnancy and childbirth. It caused 40 per cent of the 7,380 deaths included in the study." A later report for 1937 stated infection to be the cause of death in 35 per cent of cases. Sepsis has maintained a relatively level curve from 1915 to 1937[2] as a factor in maternal mortality in the United States. Deaths assigned to this cause have ranged from 24 to 18 per 10,000 live births during this period. Such reports make us realize the great importance of puerperal infection as a stumbling block in our attempts to lower the high maternal mortality rate of the United States as compared with certain foreign countries.

Another point brought out in the report is that infection, in the fatal cases, developed in the hospital in but 15 per cent. This seems to counteract the general impression that most cases of infection develop in hospitals, probably because of too great a tendency to interfere with the course of labor or abortion.

The observations of Schottmüller[3] led Drs. O. H. Schwarz and W. J. Dieckmann[4,5] to investigate the bacteriology of the cases on our service and they soon confirmed his findings. The most important point was that a group of anaerobic streptococci which had been overlooked or considered only as nonpathogenic saprophytes were really accountable for a very large percentage of cases of puerperal infection.

In a series of 246 cases[6] of puerperal infection treated on the Obstetrical and Gynecological Service of Washington University, anaerobic organisms were isolated from the uterus in 84.1 per cent. The number of deaths was thirty-one and analysis of causes is shown in Table 1.

Table 1

		Type (Colebrook)
Peritonitis	16	III
Septicemia	10	IV
Thrombophlebitis	4	II
Pelvic abscess (ruptured)	1	II
	31	

If these cases are classified on the clinicopathologic basis of Colebrook,[7] a very important point is emphasized—namely that peritonitis is probably the most serious complication of all. Septicemia may re-

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spond to various types of therapy, but when a true peritonitis develops the prognosis is most guarded.

Schottmüller stressed the relationship between thrombophlebitis and the anaerobic streptococci. We observed the same finding in our series and lost four out of fifteen over a period of five and one-half years. Since January, 1930, we have not had such a death. This is probably due to two main factors (1) prophylaxis and (2) early active treatment of uterine infections. Of late we observe only an occasional mild case of thrombophlebitis.

As stated above, we have had thirty-one deaths due to puerperal infection. Upon further analysis it is brought to our attention that thirteen of these deaths occurred among patients delivered by our service, eight of which were delivered by cesarean section.

Table II

TYPES OF ORGANISMS IN THIRTY-ONE FATAL CASES

Anaerobic streptococcus	15	(4)
Hemolytic streptococcus	7	(2)
Staphylococcus albus	7	(6)
Streptococcus viridans	1	(0)
Nonhemolytic streptococcus	1	(1)
	31	(13)

The incidence of infections due to *Staphylococcus albus* was found to be due to faulty technique in the sterilization of gloves and was soon corrected. Note the important rôle played by the anaerobic streptococcus in these fatal cases whether delivered in the hospital or outside.

Upon noticing the importance of infection as the cause of mortality following cesarean section, we undertook the study of the bacteriology of the uterus at the time of operation and correlated the findings with the use of antiseptic vaginal instillations. The antiseptic used was 1 per cent neutral acriflavine in glycerin, as described in a recent article.[8] The instillation is best given with an asepto syringe No. 2042. This syringe holds 8 c.c. (average dose) and is rubber tipped so that it can do no serious damage. An instillation is given upon admission and repeated every four hours if the patient is in active labor. In waiting cases at or near term and cases which may be delivered by section, instillations are ordered given once daily unless the membranes have been ruptured when instillations are given twice daily.

As a control group for this study we refer to the report of Harris and Brown[9] in which cultures were obtained in the same way, but no instillations were used. The contrast is very marked. In their study of fifty patients, uterine culture was positive in 44 per cent. They noted the predominance of anaerobic streptococci. Anaerobic growth was obtained in 45 per cent of the positive cultures. "No sterile cultures were obtained from patients in whom active labor had lasted for six hours or more and only one positive culture was obtained where labor had progressed less than six hours. . . . when cesarean section is definitely indicated the ideal time for its performance is at an appointed time at the end of pregnancy or at the very beginning of labor." Later in labor they suggest employment of the low cervical section or the radical procedure (supravaginal hysterectomy).

In a series of 144 cases studied at the St. Louis Maternity Hospital, the incidence of positive uterine culture was 4.1 per cent when vaginal instillations of acriflavine were employed. Anaerobic growth was present in 83 per cent of the positive cultures. Intrapartum infection accounted for 50 per cent of the positive cultures. A negative uterine culture was obtained as late in labor as 107½ hours with the use of instillations. In two cases forceps delivery was attempted before section was performed and the uterine cultures were negative. Since 1931, puerperal infection as the cause of mortality associated with cesarean section, has been eliminated, apparently due to the use of antiseptic vaginal instillations. The indication for the radical procedure of supravaginal hysterectomy because of infection has been avoided. This technique makes it relatively safe to postpone section until a much later hour in the labor

than has been recommended by other reports.

In the report on Maternal Deaths,[1] abortion was reported in 45 per cent of the deaths due to septicemia. The report for 1937[10] mentioned this proportion as 40 per cent. In the study of uterine cultures in approximately 1600 abortion cases, 60 per cent were found to be positive. Anaerobic growth was obtained in 92 per cent of the positive cultures. This again emphasizes the importance of this group of organisms in puerperal infection. Contrast this with the lower incidence of the hemolytic streptococcus, which was found in 7.2 per cent of a series of 2,042 uterine cultures.

The importance of the hemolytic streptococcus is not to be belittled for a moment when it is present and causing the disease. In the twenty deaths which occurred in a series of approximately 1600 abortions on the service of St. Louis City Hospital No. 1 between 1934 and 1939,[11] (to be reported) 35 per cent showed hemolytic streptococcus present in the uterine cultures and 25 per cent in the blood cultures (mortality 1.2 per cent).

In view of our results,[12] it seems advisable to continue the active gentle treatment of the uterine cavity, as early as possible in cases of suspected uterine contamination: (1) to obtain the diagnosis; (2) to determine the type of organism present; (3) to arrest blood loss; (4) to shorten convalescence; and (5) to avoid complications. Do not use a sharp curette in the treatment of such cases.

Posterior colpotomy is of great value in the treatment of patients who develop pelvic infections that finally point in the cul-de-sac. A word of caution should be given in regard to the handling of such cases: Wait until the process is well localized. If possible, avoid the use of general anesthesia during the procedure for fear too much force may be used and result in the rupture of such an abscess into the peritoneal cavity as has occurred in a few instances. Place a good sized T tube and allow it to remain in place long enough (usually six weeks). Such a tube should be cut spirally in order to avoid too much pressure against the vaginal wall with resultant erosion and possible perforation of the rectum.

Prevention of maternal mortality from infection will result from: (1) thorough surgical preparation of patient; (2) excellent aseptic technique; (3) proper use of masks; (4) antiseptic vaginal instillations; (5) prompt isolation of infected patients; (6) early gentle evacuation of uterine débris and establishment of adequate drainage; (7) transfusions as indicated; (8) chemotherapy when indicated.

Without the assistance of chemotherapy the maternal mortality from puerperal infection on the Obstetrical Service of Washington University has been:

	Deliveries	Deaths
July, 1924–Jan. 1932.....	9,529	13
Jan. 1932–Jan. 1940*.....	12,913	0

* Vaginal instillations used during this period.

These results coincide with the statement of Schottmüller: "Heute muss es also heisen: Die Gefahr kommt weniger von Aussen als von Innen."

TREATMENT

The use of vaccines is too slow to be of value. Intravenous dyes have proved of little use. Antitoxin helps in the treatment of specific organisms, but passive immunity with antiserum has never appealed to me. Nonspecific therapy does not seem to be indicated in acute infections. Heat may be of benefit later in the course of the disease when the patient's temperature has approached normal. After the febrile period is over many patients are found to be in need of thyroid medication due to depletion of the thyroid.

Transfusion is probably the best therapeutic agent we have available. One should be guided by the hemoglobin level and try to maintain it between 90 and 100

per cent. The anaerobic streptococcus causes marked anemia due to its proteolytic action on red cells and frequent transfusions of from 500 to 750 c.c. seem to give best results. Immunotransfusion is of value if proper donors are available.

Chemotherapy with drugs of the sulfanilamide group should not be used indiscriminately because of the possible by-effects which make the patient feel miserable and may inhibit her recovery. They also frequently mislead the physician into the belief that the patient is much worse off than she really is. When the bacteriologic findings in a given case indicate that this group of drugs might be of value, one may proceed cautiously with close observation, using the least toxic preparation available and giving moderate doses over as short a period as possible. The results of such therapy are not 100 per cent good even in patients infected with the hemolytic streptococcus. It is necessary to follow closely the effect on the red blood cells, white blood cells and hemoglobin, and to check the level of the drug in the blood stream from time to time. There is no evidence of the value of this group of drugs in patients infected with anaerobic streptococci and since these organisms most frequently are the offenders in puerperal infection, it is wise to omit sulfanilamide medication until the hemolytic streptococcus is proved to be present. It seldom is present when the obstetrical care of patients is what it should be. Perhaps later we may have some related drug which will be of more general value.

The reports of Colebrook and Purdie,[13] Morris,[14] Chandler and Janeway,[15] and Waters,[16] suggest the value of sulfanilamide and allied drugs in the treatment of puerperal infection, but their results are not very convincing since similar results are obtained without such drugs.

When a patient in the puerperal state develops signs of infection, which cannot be accounted for after the usual diagnostic methods have ruled out all other possible infections, it seems justifiable to investigate the uterine cavity. The surgical principles involved in our treatment of such cases are; (1) drainage of an infected wound site, and (2) debridement of a potentially infected cavity. This is done with a minimal amount of manipulation in order that further trauma may be avoided. We have demonstrated that this procedure can be safely performed by a junior intern under proper supervision. A general anesthetic is not used, because this would remove the inhibiting influence of the patient's response to pain which is usually indicative of two active manipulation. The patient should be under the influence of some sedative so that she is not too apprehensive. Morphia (.01 Gm.) with hyoscine hydrobromide (0.0005 Gm.) followed by hyoscine (0.0005 Gm.) in forty-five minutes is given, the second dose administered at least thirty minutes before the patient is prepared for examination.

The perineum is prepared with tincture of mercresin. The bladder is *not* catheterized because of the danger of contamination which may frequently superimpose a urinary infection. Drapes are placed. A Graves' vaginal speculum is used to obtain exposure of the cervix. If this is not satisfactory, several vaginal retractors will be necessary. The vagina and cervix are then prepared with the above solution. The cervical canal is treated with the solution and dried carefully with sterile gauze. A culture is obtained from the uterine cavity with a modified Little tube. If it is not possible to have careful bacteriologic investigation of the material obtained, several smears can be made and stained by the Gram method. This has been done routinely and found to check very well with the bacteriologic findings. Both aerobic and anaerobic blood agar slants should be made. The Wright anaerobic technique is used in the search for anaerobic organisms.

After the culture has been obtained, a gentle bimanual examination is done to determine evidence of any spread of the uterine infection, pelvic abscess or thrombophlebitis. This is also done without an

anesthetic in order that the patient's reaction to pain may limit the extent of the examination. Too much pressure might cause rupture of an abscess internally. The uterine cavity is very carefully investigated with a Foerster's sponge-holding forceps, plain jaw. Dilatation of the cervix is usually sufficient to permit this. The closed sponge forceps is inserted to the depth desired, opened, closed, and removed to see if any tissue has fallen within the jaws. The forceps should not be advanced with the jaws open, because of the danger of grasping the uterine muscle. The uterine wall is next explored very systematically and with great gentleness by means of a "uterine wiper" (formerly called a vaginal depressor) much as a windshield wiper covers the glass of a windshield, without marring the surface. (No curettage is done.)

The uterus is usually found to be relaxed in such cases. After mechanical removal of any retained débris, the patient is given an intra-uterine douche, using a Bozeman's extra large intra-uterine douche nozzle. This instrument permits the free exit of the solution from the uterine cavity without positive pressure being established. Two liters of a 1:1000 solution of potassium permanganate in sterile water at 105 to 110°F. are used. This solution is usually acidulated with 50 c.c. N/1 sulfuric acid. The bottom of the douche can is held at the level of the symphysis so that the water pressure of the solution as it enters the douche nozzle is 15 cm. or less. Such a douche results in (1) removal of small bits of tissue remaining after mechanical emptying of the cavity; (2) firm contraction of the uterus, including the cervix, so that bleeding is controlled and the sinuses are closed; (3) elimination of the putrid discharge which is characteristic of anaerobic infections. It is seldom necessary to repeat the procedure.

CONCLUSION

Puerperal infection in the early stage is primarily a surgical disease, infection of a wounded area (placental site), and should be treated accordingly. Drainage should be established early and maintained if necessary. All débris should be evacuated as gently as possible. Avenues for spread of infection should be closed by keeping the uterus well contracted. Complications are avoided by early treatment. Prophylaxis is accomplished by the early, consistent use of antiseptic vaginal instillations. These are of value in avoiding both endogenous and exogenous infection. Excellent aseptic technique with a minimum of interference by attendants will largely eliminate exogenous infection. Transfusion is of great value. Chemotherapy should be used when there is indication.

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RESPIRATORY COMPLICATIONS IN THE CARE OF THE NEWBORN*

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THE establishment of respiration is the first concern as the child emerges from the intra-uterine environment and is surrounded by air instead of by the liquid in which he has been immersed for many months. The hazard of the transition which occurs abruptly at birth is illustrated by the frequency with which injury of the respiratory system is observed at the time of delivery, since it involves an experience in obstetric pathology which is inescapable.

The numerous complications of fetal life which result in failure to survive have recently been analyzed by Potter and Adair[1] in a series of 17,000 deliveries. The present discussion is concerned with the respiratory system, especially with reference to the origin and prevention of injuries before birth.

Injuries of the respiratory system which are evident at the time of birth include: (1) asphyxia, or failure of the nervous mechanism of respiration; (2) atelectasis, or incomplete dilatation of the pulmonary alveoli; and (3) pneumonia.

Despite the common occurrence of depression and failure of respiration in the newborn and the numerous reports of autopsy examinations of the lungs of stillborn babies, there has persisted considerable obscurity regarding the pathogenesis of respiratory complications which are seen at the time of birth. Consequently, methods of dealing with asphyxia neonatorum and prevention of pulmonary damage have been largely empiric and controversy has been promoted in proportion to the variety of individual experience. It is evident that consideration of the prevention of respiratory injuries involves first of all demonstration of the pathogenesis of respiratory failure and of pulmonary damage.

Since these respiratory complications are immediately evident at the time of birth, it follows that the injuries originate during intra-uterine life. It is essential, therefore, to determine the normal state of activity of the respiratory system before birth in order to understand the mechanism by which abnormalities arise. Many difficulties attend the study of the fetus in the intact uterus before birth. It is a clinical observation that at the time of cesarean section the fetus is in a state of apnea, even though general anesthesia is eliminated and local infiltration or spinal anesthesia is used. Prolonged apnea has been regarded as the characteristic condition of the fetal respiratory system throughout embryonic life.[2] It has seemed logical that the entrance of amniotic fluid into the pulmonary alveoli must be abnormal and even result in drowning of the fetus at birth.

Experiment has thrown considerable light upon these problems. Under laboratory conditions the state of activity of the fetal respiratory system has been determined by direct observation of fetuses in the unopened uterus.[3] For instance, in rabbits in which labor has been inhibited following the addition of fresh lutein tissue in the ovaries, by the injection of extract of pregnancy urine, fetuses at full term or post mature development have been observed directly for many hours after the exposure of the uterus by laparotomy. Anesthetics were eliminated by section of the lumbar spinal cord prior to laparotomy. Observation of fetuses in the intact uterus

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under these conditions revealed striking activity of the respiratory organs in the intra-uterine environment. The respiratory movements continued for many hours at a constant level. When suitable experimental methods are employed, it is evident that the first respiration is not initiated at birth, but extends far back into embryonic life.

In the human as well as in other species, long periods of automatic activity of the fetal respiratory organs have been noted. In women the rhythmic fetal movements are transmitted through the abdominal wall and are integrated in a pattern that is characteristic of respiration. Records of the excursions of the abdominal wall have been obtained by kymograph and by motion pictures.[4]

In view of these findings regarding the normal physiologic activity of the respiratory organs before birth, it is evident that depression or failure of respiration at birth must be regarded as the suppression of previous activity rather than the failure of some new mechanism to begin functioning. The pathogenesis of asphyxia neonatorum is thus closely related to changes occurring in the intra-uterine environment. Control of asphyxia centers upon the period before birth.

The next step in the prevention of respiratory failure at birth involves recognition of the factors which cause apnea of the fetus within the uterus. If one turns to experiment in order to trace the development of the apneic state, starting with fetuses which show active respiratory movements, it is found that three main types of fetal apnea may be distinguished, namely, anoxemic, acapnic, and anesthetic. The normal regulation of fetal respiration depends upon the oxygen and carbon dioxide level of fetal blood, but differs in certain respects from that of the adult. Oxygen want depresses or abolishes fetal respiratory movements. Carbon dioxide deficit results in depression or apnea of the fetus, showing that a certain level of carbon dioxide is essential for the maintenance of fetal respiration. An excess of carbon dioxide has little effect. The fetal respiratory system is peculiarly sensitive to narcosis. Respiratory movements may be abolished in the fetus at a level of analgesia which does not impair maternal respiration. Of the three factors found to be depressant to fetal respiration, anoxemia and anesthesia stand out preëminently.[5] Acapnic depression is so readily reversible that there is little evidence that acapnia has a significant rôle in the production of permanent injury. In current reports from various clinics regarding the relation of anoxemia and anesthetics to asphyxia neonatorum additional evidence is available for evaluation of the importance of these factors.[6,7,8,9]

While prevention of asphyxia is related to an appreciation of the etiologic factors which are involved, resuscitation of the apneic child remains a large problem. Marchetti[10] has recently presented a critical survey of methods and principles which have been tested in such emergency. In a series of studies upon the maintenance of artificial respiration, Murphy[11] showed the effectiveness of the Drinker respirator in keeping up pulmonary ventilation at a level which was adequate to support life for many hours during which time the infant promptly showed respiratory failure unless artificially aided. Murphy has also emphasized the aid to the thoracic circulation which respiratory excursions exert.

Regarding the usefulness of respiratory stimulants such as alpha-lobeline, coramine, caffeine, metrazol, and cyanide, it has been difficult to evaluate various reports concerning their rôle at the time of birth, since these drugs are administered usually following labor which is complicated by various factors that may alter respiratory activity, such as anoxemia, anesthesia, and trauma. In order to determine the effect of these respiratory stimulants upon the normal newborn, we[12] have carried out experiments upon newborn rabbits immediately following delivery. Results showed that response by increase in rate or depth of breathing was

brief, lasting less than a minute. There was a narrow margin between the dosage level at which stimulation appeared and the dosage at which convulsions or death occurred. Thus with lobeline, convulsions followed a dose which was twice the minimal effective amount. With caffeine, metrazol, coramine, and cyanide, convulsions followed a dose of three times the minimal effective amount. Furthermore, death frequently followed the onset of convulsions resulting from the administration of alpha-lobeline, caffeine or coramine.

The possibility of prevention of intra-uterine pneumonia is closely related to the nature of the etiologic factors which are concerned. Outstanding among the factors which are involved is contamination of the amniotic fluid with cellular and sebaceous debris, meconium, or bacteria. The origin of abnormal amniotic fluid may be traced in numerous complications of labor, for instance, the occurrence of asphyxia and the escape of meconium into the fluid surrounding the fetus, premature rupture of the membranes, and prolonged labor. In this connection it is noteworthy that vaginal examination may introduce an additional hazard for the fetus as well as for the mother.

In evaluating the etiologic factors which are implicated in intra-uterine pneumonia it is obviously important to consider the extent to which the respiratory excursions of the fetal chest and diaphragm are effective in promoting a tidal flow of amniotic fluid between the amniotic sac and the interior of the lungs. If one resorts to experiment a clear-cut answer is obtained. For instance, in a rabbit in which the uterus was exposed by laparotomy, India ink was injected into the amniotic sacs of fetuses which were breathing as well as into the amniotic sacs of littermates in which respiratory movements had been abolished by injection of the fetuses with pentobarbital sodium. Examination of the lungs of the fetuses which had been breathing showed carbon particles in the pulmonary alveoli throughout the lungs even within one minute after the addition of the ink to the amniotic fluid. In contrast, the lungs of apneic fetuses contained none.[4]

Furthermore, the findings in the lungs which have been reported in various series of autopsies[13,14] may readily be understood in the light of the active functioning of the respiratory organs before birth. Farber and Sweet[15] found amniotic sac contents in 88 per cent of the lungs of 124 infants surviving two hours to five weeks and presented evidence of a vernix membrane coating the pulmonary alveoli in some instances.

The significance of prompt expansion of the pulmonary alveoli immediately following birth is evident when comparison is made of the changes in the structure of the lungs obtained from fetuses which have not breathed air with those of infants which have breathed air.[16] Before birth the alveoli are partly dilated, being filled with amniotic fluid. After the breathing of air, there is a rapid increase in alveolar expansion. Adequate aeration is thus provided and the newborn is not drowned, since the elasticity of the alveolar walls permits an increase in the size of the alveoli of such magnitude that the surface area now obstructed by fluid becomes relatively greatly increased.

Atelectasis may arise during intra-uterine life by the breathing of abnormal amniotic fluid containing debris which obstructs and injures the respiratory passages. In case obstruction occurs at the time of delivery, there will be failure of alveolar expansion beyond the stage normally present within the uterus.

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While the total infant mortality has been reduced from 100 per thousand live births in 1915 to 54.4 per thousand in 1937, the neonatal (first month of life) death rate as well as the stillbirth rate has remained practically untouched.
From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

OBSTETRICS AND GYNECOLOGY SYMPOSIUM

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GYNECIC PHYSIOLOGY AND THE GYNECOLOGIST*

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IN no branch of medicine today does there exist a wider hiatus between experimental advance and clinical practice than that pertaining to the physiology of reproduction in the female—the fields of gynecic physiology, on one hand, and obstetrics and gynecology, on the other. The recent advances in this field of most general interest to the gynecologist are those which enable him to appreciate best the present status of the hormonic principles already available for use, and what systemic and local changes they elicit under particular conditions. The problem of the number, nature and interrelationships of the gonadotropic and sex hormones is basic for an understanding of the effects which such substances have, and so will be reviewed summarily.†

THE GONADOTROPIC HORMONES

Status. The gonadotropic hormones are those which are capable of inducing directly characteristic changes, of a stimulating nature, in the gonads of suitable experimental animals. Recent work has established that these may be classified, at the present time, into three groups.[1,3,6,7] The basis of the distinction between the several substances is largely biological, although chemical separation (by electrophoresis of suitable extracts, or by proteolytic digestion) may render the present simple grouping obsolete within a few years. Today, the gonadotropes are held to be: (a) of anterior pituitary origin; (b) chorionic origin; and (c) those typical of pregnant mare's serum, the active principles of which probably arise from the placenta.

None of the gonadotropes has been isolated in purified form, and all are standardized biologically by methods which are not exact in themselves nor uniform in various laboratories. Despite this fact, extracts are now commercially available, which, under highly restricted conditions, are said to be predominantly "follicle-stimulating" or "luteinizing." The utility of such extracts will necessarily depend upon their true effects on the human ovary and other tissues, and *these effects may not be accurately stated at the present time* unless resort is made to specific enumeration without evaluation of endless experiments on subhuman and subprimate forms. Van Dyke, discussing the gonadotropes in his recent book on the hypophysis, says: "Despite all the labor represented by a vast number of reports during the past few years, it is not yet possible to enumerate satisfactorily the gonadotropic hormones of the pituitary. Separate follicle-stimulating and luteinizing hormones are believed to exist."

One might point out that this belief is today complicated by two important conflicting facts. First, it has been shown

† Toward a solution of the problem of interpretation of this work, a number of recent books should be helpful, particularly to obstetricians and gynecologists. On the clinical side are books by Fluhmann,[1] Hamblen,[2] Sevringhaus,[3] Werner,[4] and Lane-Roberts et al.[5] These authors do not neglect the physiological aspect of the subject, but deal better and more fully with the clinical phases. These references will stand as beacons to those who desire detailed summaries of the present status of endocrine therapy in gynecology. In addition to these, other recent books deal with more basic aspects of reproductive phenomena in the female. Among these may be mentioned the second edition of *Sex and Internal Secretions*[6] written by a group of outstanding authorities; the recent second edition of the book by Van Dyke on the pituitary gland;[7] a third book on the physiology of the uterus[8] deals especially with the endocrine and other mechanisms of uterine motility, circulation, metabolism, innervation and growth. Hartman's book on the fertile period in women[9] and Dickinson's book[10] on the control of conception stand as the authoritative references dealing with these topics.

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that a corpus luteum, which undergoes degeneration as a result of hypophysectomy (through removal of a hypothetical luteinizing hormone), may be maintained by simple administration of an estrogenic hormone.[11] Second, hypophysectomy in a pregnant rabbit (which pregnancy normally terminates because of regression of the corpus luteum in such cases) may be compensated for by administration of estrogenic hormone,[63] as in the preceding instance. This effect is mediated through continuance of the corpus luteum by estrogen and not through the agency of a "luteinizing" hormone. There clearly exists, therefore, a gap which urgently requires bridging between data showing the existence of a specific luteinizing hormone, on one hand, and some which show such a substance to be nonessential, on the other.

The foregoing considerations may seem relatively unimportant and academic to the clinician, but they are fundamental to an understanding of the anterior pituitary gonadotropes. Consequently, "rational therapy" with such substances in ovarian hypofunction must await clarification of the nature and number of gonadotropic substance. *Hence, their use at this time is empirical and should be recognized as such in the evaluation of successes and of failures.* In spite of this, they are recommended by Hamblen[2] and Sevringhaus[3] for a variety of conditions (genital hypoplasia, hypoovarianism, delayed adolescence, menarche, sterility and meno-metrorrhagia). Parenthetically, one might observe that in the early development of most endocrine therapies, the successes find their way into the literature, the failures usually do not, and where success is claimed it is frequently not established that relief would not have occurred without intervention of endocrine therapy.

The gonadotrope, prolan, now coming to be called the chorionic gonadotropic hormone, is associated with human pregnancy, or neoplasms arising out of pregnancy. It is supposed to serve the purpose of sustaining the life of the corpus luteum,[7] although this conclusion is prompted solely from the known action of prolan upon the gonads of mice, rats, rabbits and other laboratory animals. This gonadotrope has not been shown to be capable, when acting alone, of inducing luteinization in monkeys or women, and in those forms in which it does induce luteinization most readily, the placenta does not elaborate appreciable or even measurable amounts of such a hormone.

The relation of equine gonadotropes to prolan and anterior pituitary gonadotropes remains to be established,[7] along with some evidence of their clinical usefulness. Some reports have indicated recently that ovulation may be induced in women by adequate administration of equine gonotropes, although the published results to date are equivocal. Sufficient ovarian follicular stimulation has been produced in some women, however, to induce an "estrous-type" vaginal smear in selected women,[12] and pregnandiol excretion (see below) has been induced in cases of cyclic amenorrhea.

Excretion of Gonadotropes. Little may be said at this time regarding the ultimate value of gonadotropic substances in endocrine therapeusis, for the reasons mentioned above. There is no doubt that the most important aspect of current work lies in what is known of their presence in blood and urine under normal and abnormal circumstances, as a diagnostic aid. Their significance in the early determination of pregnancy (Aschheim-Zondek and Friedman tests), in the early establishment of ectopic pregnancy, and the detection of chorionepithelioma are cases in point. In such cases, the gonadotropes are present in sufficient quantity to permit the use of whole urine.

In the absence of pregnancy, the detection of gonadotropes in blood and urine requires special concentration (extraction) of the hormones. In normally menstruating women, data are conflicting, although it appears that a gonadotropic substance may be obtained in the mid-cycle, about the time ovulation is supposed to take place.

The importance of detecting anterior pituitary gonadotropes in the urine of women, however, lies not so much in the fact that it is detectable about the time of ovulation, but that it is far more abundant in urine obtained during afunctional conditions (e.g., operative castration, radiation castration, postmenopause, amenorrhea of long standing) as well as in certain hyperhormonal conditions (climacteric, irregular menses, polymenorrhea). According to Fluhmann,[1] it is seldom found (one case out of ninety-one) in hypohormonal cases (irregular menses, scanty menses, amenorrhea of short duration). The active gonadotropic substance in the urine of some menopause patients was at first thought to be follicle-stimulating only, although several later reports showed it to be "luteinizing" as well. For a detailed account of gonadotropes in various types of urine, the reader should consult the books by Fluhmann and Hamblen.

THE SEX HORMONES

Terminology and Hormones. There is probably no recent achievement in gynecic physiology of more direct value to the gynecologist than the clear establishment of the exact chemical nature and probable number of the sex, or gonadal, and related hormones. The number of native hormones is now known to be few, and these lend themselves to grouping into (a) gynecogenic substances, comprising both estrogens and progestogens, and (b) androgenic substances. The structural formulae of these and other important related substances are shown in Figure 1.

Types of Response to Gynecogens and Androgens. The actions which these substances have are so generally known that they scarcely require comment.

In a limited sense, an *estrogen* may be defined as a substance derived from natural, artificial or synthetic sources, which brings about in immature, ovariectomized or senile female animals growth of the accessory sexual glands, uterus, tubes, vagina and breasts to normal (mature) or supernormal size. They are called estrogens since they are capable of simulating the specific histological and functional changes characteristic of estrus in certain laboratory animals.

A *progestogen* (Abarbanel[13]) is a substance which, acting upon a uterus first stimulated by an estrogen, causes further growth, marked glycogen deposition, secretion of the uterine glands, and hyperplasia of the glandular epithelium and of the muscular elements of the myometrium. All these changes are preliminary to, and necessary for, implantation and the maintenance of gestation, whence comes the name "progestin" devised by Corner and Allen. Progesterone also brings about relaxation of the pubic ligament, an effect heretofore attributed to a hypothetical hormone, "relaxin."[14]

An *androgen* is a substance which, when injected into an immature or castrated male animal, elicits extensive growth of the seminal vesicles, spermatic cord, prostate gland, penis, and Cowper's and the preputial glands. Such facts as these, however, are well known and fuller details are readily available to those who want them in modern textbooks of physiology, obstetrics and gynecology.[65,66,67,68]

Potency of Estrogens. Other important facts concerning the relative potencies of various estrogens are not so well-known, however. Generally speaking, the several primary estrogens are, almost without exception, *qualitatively* identical in their effects, yet striking *quantitative* differences between them have been clearly established. Such differences are clinically important because they affect not only the time of onset (latent period) of a given response but also the amount of hormone (m. e. d.), and the duration of the response which a given mass of hormone will elicit. The latter is particularly important, clinically, since it governs the frequency with which the hormone must be administered. The following considerations show the difficulties which confront us since quanti-

tative differences in estrogenic potency were established.

When the relative effectiveness of a number of estrogens was tested (uterine growth test), the following series was obtained[15] in decreasing order of effectiveness per unit mass of hormone: estradiol > estradiol benzoate > estrone > equilin > equilenin > estrone benzoate > estriol. Of these, estradiol, estradiol benzoate, estrone and estriol are commercially available, along with other estrogens. The order of this series is not basically important, however, because estriol, last in the series above, is the most potent estrogen when taken by mouth.[2,6] This is so because such a large proportion (up to 95 per cent) of other estrogens is inactivated when taken by mouth.[16]

Still another example of the difficulties encompassed by recognition of quantitative differences exhibited by various estrogens is shown by comparison, for example, of the relative strengths of estradiol, estradiol benzoate and estradiol dipropionate. Determination of the threshold dose (m. e. d.) of each of these substances for induction of estrus shows that estradiol is about twice as effective (by mass) as either of the other two substances. If, however, one considers the *duration* of the estrus induced by the same threshold mass of each hormone, the dipropionate ester is many times more effective than estradiol, while the benzoate ester is intermediate in this respect.[17] Many similar instances involving other estrogens and other tissue responses could be cited to corroborate the above points. All of them tend to show that, as our understanding of the chemical moieties of the sex-sterols has increased, standards for comparing their relative effectiveness have not been evolved.

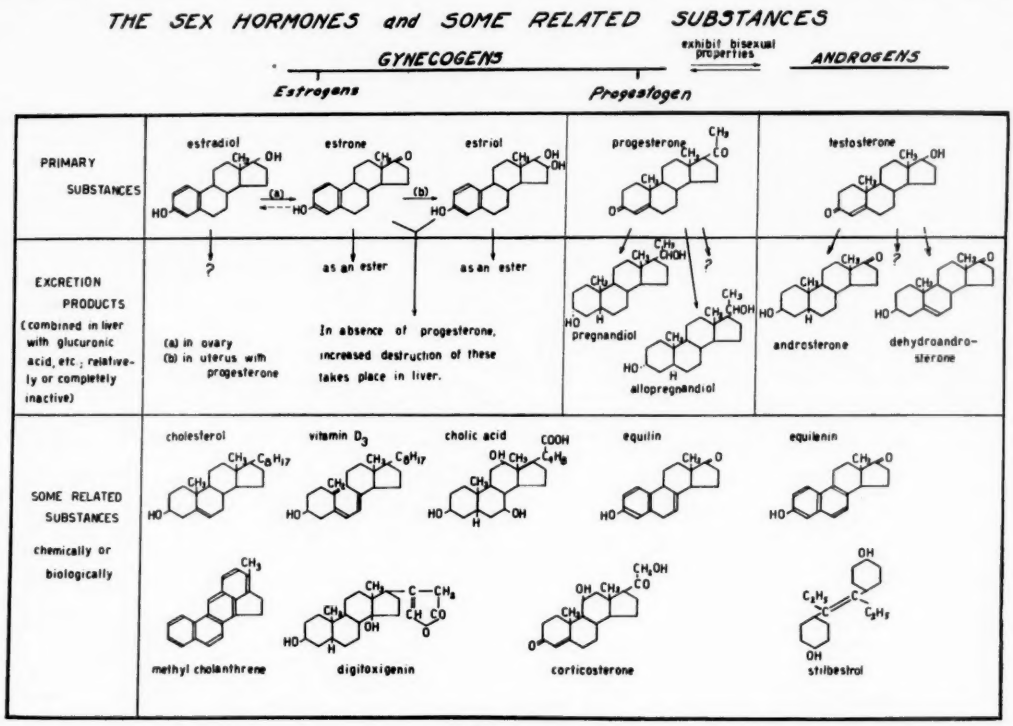

Fig. 1.

The foregoing considerations show clearly the futility of attempting to gauge the relative potency of several estrogens on the basis of one phase of a twofold response—threshold and duration. On the other side of the problem, the question of route of administration, vehicle, and frequency of injections is equally important,[49] although in the work just cited, these factors were constant; only the hormone varied. In order to include the variables of threshold and dura-

tion of the response to estrogen in a single term or unit, Miescher, Scholz and Tschopp have suggested[17] the concept of the "work-output" and "activity coefficient" of an estrogen. This is based upon measurement of the area bounded by a standardization curve (uterine weight versus days) for a given preparation, and comparison of this planimetrically determined area with a similar area for any other preparation. The "coefficient of activity" is then expressible by calculating the ratio of one work-output to another work-output. Despite the obvious merit of such terms, this suggestion has not been generally adopted. Use of it would make it possible for the gynecologist to compare the estrogenic activity of one hormone with that of any other, a feat which is impossible by the present ambiguous standards.

This state of affairs requires one further word of explanation for those who confidently employ five or ten thousand international or rat units of an estrogen—any estrogen—in practice. The crux of the situation lies in the fact that two *different* international units have been formulated by the Committee on Hygiene of the League of Nations, one for estrone and one for estradiol benzoate. The "international unit" is 0.0001 mg. of each substance. In accordance with this, ampules of each will be labelled with the same number of *international units*, when the same amount, by mass, is in each. Nevertheless, by the Allen-Doisy rat test, or by the uterine growth test, estradiol benzoate is about one-half as potent as estrone in m. e. d., but it gives a much more prolonged response than the latter. Moreover, no international unit exists for most types of available estrogens (only estrone and estriol are listed in New and Non-official Remedies, 1939). Clearly, dosages of estrogens for clinical use based on such an artificial distinction are worthless to the physician.

The clinician may well ask what he is to do to obtain greatest effectiveness from a given dose, when the label on the box gives no true indication of the relative potency of its contents. The answer is not easily given. The entire question of standardization should be reopened by the proper authorities, and a true basis for comparison agreed upon. In the meantime, the physician would do well to adopt some one type of estrogen in his practice, learn by experience how much and how frequently it must be given to obtain a desired effect. He would do well, perhaps, to be guided by the fact that esterification usually prolongs the action of an estrogen, while reducing its threshold for induction of estrus.

BISEXUAL POTENTIALITIES OF THE SEX HORMONES

As the atomic structure of the sex hormones and related sterols was established by a succession of brilliant studies in different laboratories and in various countries, our understanding of the nature of their effects in the mammalian organism became known. Broadly speaking the results showed bisexual effects of the hormones, although it was recognized that the several gynecogens and androgens exhibit a special predilection for specific reproductive tissues in females and males, respectively. The bisexual character of the hormones is suggested by studies of sex hormones in the urine of men and women and by the effects of injection of these hormones into both sexes.

Gynecogens and Androgens in Urine. In the urine of both men and women, gynecogens and androgens are found. A number of recent studies have been made on this and related topics, but those of Koch[18] may be cited as illustrative of the point as it is understood today. In men, there was found to be the equivalent of 4.0 mg. (40 international units of androsterone) per day excreted in the urine with an average daily excretion of estrogen amounting to 0.001 mg. (10 international units of estrone) in the same urines. Similarly, the urine of women showed appreciable quantities of both substances: of androgen, the equivalent of 2.6 mg. (26 international units of androsterone) was found, along with an

average daily excretion of estrogen equivalent to 0.0026 mg. (26 international units). Although two peaks of estrogen excretion occur during each normal (ovulatory?) menstrual cycle, no correlation was observed in the amount of androgen excreted at these same times (mid-interval and premenstrually). Androgen was found to be unusually high, however, in the urine of women with hypertrichosis.

The identity of the urinary androgens and estrogens has not been fully established. More will be said of these urinary estrogens below. Concerning the androgens, Koch says: "We know that androsterone and dehydroandrosterone are present in men's urine, but what relative amounts of these two substances are, is not known. Nothing definite is known as to the nature of the androgens in the urine of non-pregnant women." With regard to the estrogens, he says, "We are equally uncertain as to the chemical nature of the estrogens in men's and non-pregnant women's urines. The estrogenic material in men's urine however, shows the biological characteristics of theelin (estrone) and not of theelol (estriol)."

Bisexual Actions of Injected Hormones. The bisexual properties of a number of gonadal hormones have been investigated under a variety of conditions. The most extensive and systematic experiments are those of Korenchevsky[19] and his associates. The situation has been succinctly stated by him as follows: "These experiments on gonadectomized rats have established that nearly all the sexual hormones investigated tend to a greater or less degree to restore to normal both the male and female sexual organs, which have atrophied as a result of gonadectomy: a striking example is the most powerful of the male sex hormones, testosterone propionate. This brings about a return to normal, or even supernormal, of the atrophied sexual organs of castrated males. The same hormone also restores the structure of the atrophied uterus and vagina of an ovariectomized female to a condition not far from normal, while the weight of the vagina and the development of some of the tissues of this organ is even supernormal. In normal rats, it stimulates the development of the uterus and vagina to much above the normal size and weight."

The relative effectiveness of the hormones, acting alone, in stimulating female sexual organs is as follows: estradiol > estrone > testosterone propionate > testosterone > androstanediol > androstenediol > androstendione > transhydroandrosterone > androsterone > progesterone. When the last named, progesterone, is administered with suitable amounts of estrogen, however, it compares with estrone and estradiol as a gynecogen. It is, moreover, to a certain degree androgenic, for under suitable circumstances it maintains or stimulates the prostate gland and seminal vesicles of castrated male rats. These accessory organs display secretory activity under such circumstances.[64]

Other, less direct, kinds of evidence have been adduced which demonstrate the bisexual potentialities of the gonads. An example of this is found in the observation that transplants of ovarian tissue into the ears of castrated male rats will sustain the accessory organs of reproduction, but not if the transplant is made into the warmer environment of the body. Vicarious gonadal function is not restricted to rats and lower animals. Thus, report was recently made[20] of a "perfectly formed and beautiful woman who possessed gonads which proved structurally and anatomically to be testes." The bearing of such conditions on varying grades of intersexuality is obvious, and they raise a question of whether hormone tests of blood and urine should be regarded as decisive diagnostic aids when corrective operations are contemplated. It is well-known that the surgeon's knife can oftentimes correct certain types of intersexuality. One can hardly refrain from making the observation in passing, however, that, quite aside from the correction of abnormal structure in sexual organs one ought also to consider the mental and social readjustment demanded of an individual

after the "corrective" operation is performed. In one classic case (masculinization from an adrenal tumor) studied by Young,[21] an individual who, in appearance, mental attitude, and sex-behavior was a male, possessed rudimentary female generative organs. When confronted by the decision that his sexual organs were potentially female, and that marriage with religious sanction to a woman was therefore out of the question, he chose self-destruction rather than undergo the mental and social reorientation which the necessary operation entailed.

From the standpoint of therapeutics with androgenic hormones, a number of recent reports suggest that testosterone or testosterone propionate may be useful in gynecological practice. The conditions in which it has been used successfully are: cyclic mastalgia, functional uterine bleeding, essential dysmenorrhea, premenstrual tension, the menopause syndrome, and relief of after-pains. In general, these reports are very favorable, and some are well-controlled. If, then, androgens are to become part of the armamentarium of gynecologists, one should question the wisdom of using a powerful agent which changes the voice, grows a beard, and may give rise to a masculine type of skeletal musculature and of mental outlook. The clinical reports now available frankly warn against such dangers. It is as yet too early to state what dosages may be employed safely in any given case and yet be therapeutically effective. It appears that masculinization may be detected[22] if dosages of some 500 to 600 mg. of testosterone propionate are used in a given course of treatment lasting some two weeks (as in the treatment of functional uterine bleeding); some reports[13, 23] indicate that much smaller doses (40 to 60 mg.) may be effective in this condition without any undesirable side reaction. It may be pointed out that the principal factors which govern the level of androgen at which masculinization will be detected in any given case are not known. Consequently, androgen dosage must for the present be empirical, and its effectiveness will depend upon the individual susceptibility of the patient to the hormone.

The problem of the ultimate utility of androgens in clinical practice therefore remains to be established. Any rational therapeutic efforts in this connection will take into account, however, the established effects which testosterone has upon the female organism. In the uterus of suitable rats, testosterone gives rise[19] to irregular structure of the stroma, vacuolation of the uterine epithelium, mucous cystic development of the endometrial glands, and an abnormal abundance of fibrous connective tissue in the myometrium. In the vagina, this hormone elicits deficient or irregular mucification, persistence of a narrow epithelium, and at best, only slight cornification with dropsical vacuolation and leucocytic invasion. In addition, testosterone causes growth of the clitoris, and marked development of periurethral glands into a "typical prostate." Still other important actions of androgens in the female have been established. For example, it will prolong gestation (i.e. inhibit parturition) in rats, and will prevent abortion after ovariectomy during pregnancy in lower animals, just as progesterone will do.[8] Also like the luteal hormone, it will inhibit menstruation in monkeys and women, and in rabbits, it will elicit progestational proliferation of the endometrium and will inhibit tubal and uterine motility. The most striking difference between testosterone and progesterone lies in the fact that the latter is much more efficient than the former; for certain of the above responses, a fivefold difference has been demonstrated. The systemic effects of androgens in the female resemble some of the systemic effects of estrogens. Thus they give relief from the vascular disturbances of the menopause and in many cases, they give rise to a general feeling of well-being.

At the present time it is impossible to visualize the rôle of androgens in the etiology of specific gynecological pathology, other than in cases of intersexuality, as

noted above. The fact that such substances are normal excretory products in the urine of women leads one to surmise, as Korenchevsky has done, that failure to consider the possible interplay of gynecogens and androgens is the basis of the failure, in the past, to interpret correctly the endocrine basis of a variety of common gynecological conditions. It is probable, therefore, that this new phase of gynecic physiology, which today complicates the problems of all who are engaged in this field of endeavor, will be tomorrow a stepping stone to the ultimate simplification of our understanding of the physiology of the sexual and reproductive cycle.

ARTIFICIAL ESTROGENS

Stilbestrol. A word must be said about a topic of increasing interest to, and discussion among gynecologists, namely, that of the status of artificial estrogens. Within the past few years, a number of substances have been obtained which bear no structural resemblance to the natural estrogens, i.e., no sterol nucleus (Fig. 1), yet they are highly estrogenic. Qualitatively, some of these substances compare with the natural estrogens in potency. The best known of these is stilbestrol. Some substances, it has been pointed out, are estrogenic only as regards certain limited aspects of the estrous response, and hence should be regarded as pseudo-estrogens. Stilbestrol, however, appears to be a true estrogen, according to the above definition, since it differs from natural estrogens in no important way in its biological effects on the female genital tract.

In view of the very low cost of production of stilbestrol in large quantity, and in view of its very high potency (especially when administered orally) and its similarity of action to natural estrogens, this substance lends itself readily to commercial exploitation. A considerable number of clinical reports are already in the German, English, and more recently, American literature.[24,25,26] The difficulty in appraising this literature lies in the highly contradictory claims that have been advanced by various workers. There is no apparent basis for the divergence of views, and the Council on Pharmacy and Chemistry has been obliged to refrain from expressing an opinion on the acceptability of stilbestrol at this time.

All reports agree that stilbestrol is a very potent estrogen in women; that it is highly efficient when given by mouth, being but little inactivated in the processes of absorption and utilization (as natural estrogens are, especially in the human); that it is an effective agent in reducing the number and severity of menopausal flushes, and that it simulates natural estrogens in other important respects. There is *not* agreement, however, regarding the incidence of toxicity nor in the toxic manifestations which it elicits. The reserve which the American Medical Association maintains concerning stilbestrol is shown in the following partial quotation from a recent editorial.[27]

"The reports as to the toxic reactions of this substance are quite conflicting, some investigators stating that gastric distress is the only complaint, that this is experienced by from 5 to 10 per cent of the patients, and that it vanishes after a few days of administration Others have found side reactions in greater numbers. One group of American investigators has observed as high as 80 per cent of the patients exhibiting untoward reactions, including cutaneous eruptions, psychosis, lassitude and liver damage. Apparently a thorough investigation of this compound is in order before it can be prescribed for routine therapy.

"The conflicts of reports on these substances and the opinions of some authorities on the possible harm from estrogen therapy should warn against long continued and indiscriminate therapeutic use of estrogens. Like numerous other therapeutic agents estrogens are effective under proper circumstances, but there may be definite danger when they are used unscientifically. In this connection the possi-

bility of carcinoma induced by estrogens cannot be ignored. The long continued administration of these proliferating agents to patients with a predisposition to cancer may be hazardous. The idea that estrogens are related in their activity only to the sex organs should be abandoned. Other tissues of the body may react in an undesirable manner when the doses are excessive and over too long a period. This point should be firmly established, since it appears likely that in the future the medical profession may be importuned to prescribe to patients large doses of high potency estrogens, such as stilbestrol, because of the ease of administration of these preparations."

SYSTEMIC EFFECTS OF ESTROGENS

The sex hormones are quite generally, though mistakenly, regarded as having effects which are confined to the secondary sex organs and to the development of secondary sex characters about the time of puberty. Such a view neglects the fact that these hormones may have other actions and that these, in turn, may have desirable therapeutic effects, or possibly undesirable ones; this will depend upon the nature of the effect and the condition of the individual. Such a view also fails to take account of the fact that the chemical configurations of the sex hormones bear a close relationship to a number of other physiologically and pharmacologically important substances. Examples of these are the life-sustaining adrenal cortical hormone, corticosterone, bile acids, ergosterol and the active vitamin D compounds, certain carcinogenic coal tar derivatives (e.g., methyl cholanthrene), and the active portions of some of the digitalis alkaloids. (Fig. 1.) It is safe to predict that the better-known systemic, or general, effects of estrogens, enumerated below, constitute but a small part of the total effects which these substances have throughout the body.*

Cardiovascular System. The chief clinical use of estrogen for its general effects is in the treatment of the vascular disturbances of the menopause. While there is doubt about the specificity of its action in some cases, there is no question about the specific nature of the relief which it affords in the majority of cases. The basis for its effectiveness in the treatment of menopause conditions is not yet known. It has recently been established, however, that estrogens have a marked peripheral vascular action in some individuals and that this may be related to their therapeutic action. The evidence is both experimental and clinical, and may be reviewed summarily with profit.

While it is generally recognized that estrogens are without discernible effect upon the mean level of arterial blood pressure, or upon the heart, there is evidence that they have a vasodilating action on the smallest blood vessels in certain parts of the body.[8,28,29] The following facts suggest this: the injection of estrogen causes swelling and changes in the water content of the sex skin in certain primates; estrogen causes engorgement of the blood vessels in the nasal mucosa (see below); the injection of estrogen in the human is followed by a fall in capillary pressure and dilatation of the nail bed capillary vessels; estrogen causes a decrease of venous pressure in the hand; and, finally, estrogen causes a change in the water content of the skin of the rat within a few hours, qualitatively comparable to that occurring in the uterus and vagina.[8] More recent work shows that in a group of human males, estrogen likewise causes vasodilatation. The general features of the response are as follows: Within three to fifteen minutes, the volume of the finger begins to increase, sometimes after a transient vasoconstriction resulting from nervousness at the time of injection; the finger volume becomes steadily larger for at least half an hour,

* Among such other effects may be mentioned those of the relation of estrogens to certain allergies (Baker in *Canad. M. A. J.*, 40: 385, 1939); to polyarthritis (Radnor, in *Brit. M. J.*, 1:505, 1939); and to susceptibility to infection (Sprunt and McDearman, in *Endocrinology*, 25:308, 1939).

although more often the period of change lasts from forty-five minutes to an hour. The finger stays large for a period in excess of the maximum time of observation (two hours). The average percentage increase in finger volume was 4.6, although some 50 per cent of the finger is non-fleshy and so does not participate in the response.

The site of the vascular action of estrogen has been deduced from a number of related facts, all tending to show that the vasodilatation resulting from administration of estrogen involves the smallest blood vessels of the skin, namely, the capillaries and venules. For example, if arteriolar dilatation were involved, an increase in the rate of blood flow would occur and this should bring about an increase in the temperature of the skin, but such is not the case. Moreover, direct observation of the nail bed capillaries has shown that the smallest vessels are involved, although systolic and diastolic levels of blood pressure in the brachial artery are unaffected. This result could be accomplished in normal subjects only by vasodilatation beyond the arterioles. Finally, direct observation of the action of estrogen in the ear of the rabbit shows that vasodilatation involves the smallest vessels lying beyond the arterioles.[29] Since the condition of these vessels is not affected by denervation, the vasodilating action of estrogen in susceptible individuals must be mediated by some direct mechanism. It would appear to be significant in this respect that atropine inhibits the vascular effect of estrogen on the vessels in the rabbit's ear.

These vascular changes could hardly take place without some effect upon the heat regulating mechanisms of the body, since the chief function of the blood vessels in the human skin and in the ear of the rabbit is to assist in the regulation of heat loss by radiation.[8] Consequently, shifting blood into the skin (a shift must occur inasmuch as the peripheral dilatation occurs without a perceptible effect on blood pressure) should alter the capacity of the body to lose heat with less need of sweating, especially under circumstances where nervous instability or increased heat production are concerned (e.g., emotion, excitement, effort). This is especially true of the rabbit where sensible sweating (i.e., perceptible water loss) does not take place and where the loss of heat from the body occurs largely in the ears. No appreciable change in skin temperature has been found in the human following administration of estrogen, signifying that the volume of blood in the skin increases without appreciable alteration in the rate of blood flow. In the rabbit, however, marked changes in the temperature of the ear occur, varying with the room temperature and the rectal temperature of the rabbit at the time of injection. Accordingly, the blood flow in the ear of the rabbit varies, not with the degree of vasodilatation, but with the requirements for heat loss which dilatation of the smallest vessels imposes on the normal temperature-regulating mechanisms under different experimental conditions.

The mechanism by which the vasodilating action of estrogen is exerted in the skin vessels of humans and rabbits has not been established. Some facts of an indirect nature support the idea that it may be associated with an increase in the tissues in the concentration of acetylcholine.* Among these is the observation that the vasodilating action of estrogen in the ear of the rabbit can be inhibited by means of atropine, just as the hyperemia which estrogen induces in the uterus may be inhibited by means of this drug. Moreover,

* Acetylcholine is a substance of great physiological importance. It appears to be liberated at motor and certain autonomic nerve endings by the arrival of nerve impulses. At these points, it is believed to constitute the excitatory agent between the nerve and effector organ, just as sympathin is known to do in certain parts of the thoracolumbar portion of the autonomic nervous system. Acetylcholine may be inhibitory, as in parasympathetic nerve effects on the heart and on certain blood vessels (i.e., vasodilatation), or it may be excitatory, as in vagus nerve effects in the gastrointestinal musculature. The work to which reference is made above is the first to show that certain hormonic effects may be mediated by acetylcholine (i.e., they are cholinergic effects).

it has been found that, within an hour after administration of estrogen to rabbits, the acetylcholine content of the uterus increases appreciably. This coincides with the onset of a pronounced vasodilatation in the uterus. Since this effect can be elicited in a uterus which is disconnected from the central nervous system (i.e., transplanted), and since the dilatation in the ear of the rabbit involves vessels whose activity is not affected by denervation, the dilating action of estrogens on the blood vessels of certain parts of the vascular tree is mediated by the setting up of local metabolic changes within the tissues in or around these vessels. Such changes involve, in one way or another, an increase in the amount of effective acetylcholine on the blood vessels.

The consequences of these vascular effects of estrogens upon the cutaneous circulation remain a matter of speculation. These vessels, it was noted above, are primarily concerned with heat loss from the body. Because of this, the view has been advanced that at least a partial explanation of the beneficial effects which estrogen exhibits in treatment of the vascular disturbances of the menopause is to be found in increased radiation of heat from the body.[8,28] This should minimize the need for intermediation of nervous factors, which result in sweating, and periods of temporary arteriolar dilatation, as occur in the menopausal flush. The basis of relief with estrogen is broader than this, however, since a large part of the improvement one sees lies in the regression of depressed mental states which are sometimes alarming.

The Nasal Mucosa. There is one other type of evidence that bears upon the peripheral vascular action of estrogen in the human, namely, the variations in color and thickness of the nasal mucosa under the influence of estrogen.[8,30] Periodic congestion of the nasal mucosa takes place in most women, varying in intensity in different subjects. Similar effects have been produced in monkeys treated with estrogens, and the response compares in intensity of color with that which occurs during the normal menstrual cycle in this animal.[31] Recent work shows that the hyperemia of the nasal mucosa is probably associated with an increase in the effective amount of acetylcholine present. In the first place, acetylcholine is found in increased amount in nasal mucosa (in cats and rabbits) after injection of estrogen[32] and in the second place, patients with atrophic rhinitis may be successfully treated with estrogen, or, failing that, with prostigmine.[20] This drug specifically inactivates the enzyme cholinesterase, hence allowing acetylcholine to be free to exert demonstrable vasodilatation.*

Uterine Hyperemia. Mention may be made in passing of the relation of the initial hyperemia which estrogen induces in the uterus to its other uterine effects.[8,33] Within twenty minutes to half an hour, dilatation of the uterine blood vessels is maximal, the vessels become increasingly permeable and water commences to accumulate in the tissues, especially in the endometrium. Afterwards, the oxygen consumption of the tissue increases, attaining a maximum level in about twenty-four hours. By this time too, the myometrium contracts intermittently, and mitotic proliferation of certain of the tissue elements begins. It thus appears that acetylcholine is a vasodilator substance acting upon the uterine tissues which are non-motile, which possess a low level of metabolism, and in which the blood vessels are of small caliber at the outset, so offering resistance to the rapid flow of blood through the tissue. By means of the initial vasodilatation in the uterus, a ready access of estrogen to the tissues is assured. Subsequently, other, anabolic effects of the

* One should not conclude from the above discussion that estrogens will be found beneficial in the treatment of essential hypertension, Buerger's disease, Raynaud's disease, acrocyanosis and intermittent claudication. Some clinicians are coming to feel that estrogen may relieve incipient hypertension associated with the onset of the menopause, although it definitely is without effect on well-established or advanced hypertension. In the latter type of case, however, estrogen will relieve completely, or to a large degree, the flushes and involutional melancholia of menopausal origin.

hormone are effectively exerted upon the uterus.[34]

Blood Constituents. There is little published work on the true effects of sex hormones on the formed and unformed constituents of the blood. There exists, however, an abundance of data dealing with the blood picture during the menstrual cycle and pregnancy.[1] The situation is difficult to summarize, so conflicting are the various reports. These deal with an indicated decrease in the concentration of calcium, potassium, cholesterol, iodine and lecithin premenstrually. Other studies consider blood glucose, blood volume, hemoglobin, red blood corpuscle count and size, platelet count, and coagulation time. Concerning all these, Fluhmann aptly says, "The whole subject requires careful revision, and many published reports, presenting only a distorted view of the problem must eventually be discarded as useless. This criticism is particularly justifiable as applied to clinical studies because many authors have reached conclusions on totally incomplete and uncontrolled observations." The differences between males and females that are known to exist with respect to blood volume, red blood cell count and red blood cell size during puberty and later, suggest that investigations into the nature of these functional differences will prove fruitful.

Oxygen Consumption. In connection with the general oxygen metabolism, it is commonly recognized that sex differences exist. The greatest intra-individual differences occur in the female, the greatest inter-individual differences in the male. The reasons for the difference between males and females respectively have never been established.

With regard to levels of oxygen consumption during the menstrual cycle, recent work shows many contradictions.[1] This is exemplified by the following general claims regarding the rate of oxygen consumption during the menstrual cycle: (1) that it increases before and during menstruation; (2) that it increases before menstruation; (3) that it decreases during menstruation; (4) that it decreases during menstruation and increases in the early interval; and (5) that it varies in no regular way.

If the relation of total oxygen consumption to the menstrual and sexual cycle is not clearly understood, it is, however, established that the sex hormones have marked and characteristic effects upon the metabolism in certain specific tissues. In animals, Victor and Andersen[35,36] and others[37,8] have made careful studies on the oxygen consumption and aerobic and anaerobic glycolysis of a number of isolated tissues of rats and mice in controlled sexual states. Among the tissues studied are those of the anterior hypophysis, liver, ovary, uterus, kidney, and a number of endocrine glands. The uterus exhibits periodic fluctuations in the levels of oxygen and glucose consumption. The significance of these changes cannot be stated at this time.

It is probably more interesting to clinicians that the uterus is but one of several organs exhibiting cyclic fluctuations in metabolism. Thus, the liver, ovary, anterior pituitary, and thyroid tissues all show periods of high oxygen consumption and of anaerobic glycolysis.[36] In pro-estrus, estrus, and during parturition (rats), the metabolism of these organs is higher than at other times. These cyclic fluctuations are abolished by spaying, and they may be simulated by injection of estrogen. The anterior pituitary gland responds first to the hormone, the thyroid second, and the liver third. When, therefore, Graafian follicles are rapidly maturing, the respiratory metabolism of a number of tissues in the body rises to a maximum. In view of the established histological relationships between the anterior pituitary gland and the ovary, on the one hand, and between the ovary and the uterus, on the other, it is probable that the heightened metabolic processes of the pituitary bear a causal relation to the concurrently elevated metabolism in the uterus. Because of the

rôle of the liver and a number of other tissues (thyroid, adrenal cortex, and isles of Langerhans) in carbohydrate metabolism, the periodic changes in carbohydrate metabolism in the liver may well contribute to the selective burning of carbohydrates in the uterus during estrus, as well as in other tissues.

The relationships, supposed and established, between sex hormones and fat metabolism lie beyond the scope of this article.

Water and Salt Balance. Not the least of the numerous effects of the sex hormones is their influence upon the water and salt content of various tissues. Just preceding the time of menstruation one may frequently observe a generalized edema, an increase in capillary fragility and a retention of sodium chloride.[1,8] Approximately one-third of normal women gain up to 3 or 5 pounds during the premenstruum. Soon after the onset of menstruation, there is return to normal weight. Careful studies on pregnant women have established that the water retention which occurs at this time is associated with retention of sodium chloride.[38] This is favored most particularly by estrogens, and involves tissues generally.

This fact is important, since current teachings in physiology hold that sodium in the body is almost entirely extracellular while potassium is largely intracellular. Moreover, when salt is retained by the tissues of the body there is marked water retention. Some individuals show a far greater dropsical tendency than others, for unknown reasons.

The effects which the gynecogens have on water and salt retention in tissues is shown by the strikingly opposite actions which estrogens and progestogens have in animals showing adrenal insufficiency. Progesterone, like corticosterone, will sustain life in, and restore moribund, adrenalectomized animals. Estrogens, on the contrary, are toxic under similar circumstances; they serve to hasten a crisis which only administration of large quantities of sodium chloride or injection of cortical hormone or progesterone will relieve.[39,40]

No satisfactory explanation of these observations has as yet been made. They clearly point to the fact that the sex hormones, like the adrenal cortical hormone, contribute to those conditions now known to govern the water and electrolyte pattern of inter- and intracellular fluids. How this is achieved no one yet knows, although various theories suggest either that (1) the hormonic effect involves a primary regulating action on blood volume; (2) the permeability of endothelial tissues may be primarily affected by steroid hormones; (3) they have a "prepotent" action on carbohydrate metabolism; or (4) two or more of the above, along with other (endocrine?) factors may be involved.

The effect of estrogens in particular on the water content of tissues has been demonstrated in the case of the uterus (rat and monkey) and certain other tissues, especially skin and subcutaneous tissues.[41,42,43] When this hormone is injected into ovariectomized animals, the water content of the uterus increases measurably within six hours, after which a relatively greater increase in dry weight occurs. The first effect of estrogen, therefore, is to increase the amount of water in the intercellular phase of the uterus. This is nice confirmation of the histological interpretations of many workers, and it shows that, whatever its purpose may be, an increase in the amount of protoplasmic substance of the uterus is preceded by an appreciable hydration of the tissues.

Very careful measurements of the amount of water in the uterus of the monkey during selected periods of the menstrual cycle show that the changes in water content involve the tissues of the uterus as a whole, although the effects are most pronounced in the endometrium. In general, it may be said that, as the luteal phase advances, a reduction takes place in the water content of the mucosa of the corpus uteri, being most marked on the first day of menstrua-

tion (see below). In the mucosa of the cervix, changes in water content are not pronounced. Although there are a number of conditions which contribute to the lack of a marked change in this region, it is pertinent to point out that menstruation involves only the endometrium of the corpus uteri, the cervix contributing nothing to the flow.

Along with the changes in water content of the uterus are other, equally marked, changes in the electrolyte pattern of the uterus. Present data show that in the follicular phase (rabbit), the concentrations of sodium and calcium are at a maximum, the potassium and magnesium at a minimum. In contrast, during the luteal phase, conditions are reversed. The functional significance of these changes is a matter of speculation.[8] For the present, it is sufficient to note that the several sex hormones produce effects upon the retention and partitioning of water and specific ions in the make-up of uterine tissues.

All in all, therefore, these hormones, and the estrogens in particular, may be said to possess characteristic actions upon both uterine and certain systemic tissues. As in the case of the peripheral vascular action of estrogens, it appears that those effects which are well known and pronounced in the reproductive tissues are reflected in miniature throughout other parts of the body. To what extent considerations such as these should be considered in the treatment of obstetrical and gynecological problems (e.g., toxemias of pregnancy) only time will tell.

Skin Pigmentation. At the present time, only the following fact is known for a certainty concerning the relation of sex hormones to pigmentation in the skin: If hypogonadal individuals (male or female) are exposed to sunlight, they fail to tan readily although an invisible change takes place in the tissue. Thus, if androgens or estrogens are injected subsequent to exposure to ultraviolet light (up to several months) pigmentation of the skin occurs without further exposure to light. Injection of the hormones into non-photosensitized individuals fails to elicit pigmentation.[44]

The relation of this phenomenon to the mechanism of carotene and melanin deposition is unknown. It is perhaps suggestive that the sex hormones have a sterol nucleus somewhat similar to that of adrenal cortical hormone, in the absence of which coloration of the skin characteristic of Addison's disease takes place.

The reported beneficial value of estrogens in some types of acne may ultimately find its basis in connection with some of the underlying skin metabolism and vascular changes mentioned above.

Oxidation-Reduction and Sex Hormones. Reference is made to this topic to call attention to a phase of uterine physiology which, because of its relation to the very life of tissues, is important in health, and so in disease. There is little one may say at this time, however, regarding the presence of specific enzyme systems of the uterus and other tissues on which the sex hormones act in order to regulate the necessary energy for various aspects of uterine functions. In the case of the uterus, energy is required for such diverse phenomena as growth (including hypertrophy and hyperplasia), repair of tissue, secretion, activation and inhibition of myometrial motility and finally, sensitization of the mucosa for the decidual reaction.

Two enzyme constituents of the uterus, ascorbic acid (vitamin c) and glutathione, have been specifically investigated.[8] Ascorbic acid is present in the uterus when active mitotic proliferation is under way. The concentration of glutathione bears an inverse relation to ascorbic acid: it is present in lowest concentration in the proliferative stages, and highest at other times (rabbit). Studies by Pincus and his associates have established that glutathione is necessary for the phase or phases in early pregnancy of tubal and uterine function in which the life of the ovum is sustained by secretory activity of the lining epithelium of the genital tract; for this, progesterone is necessary.

At present, these and related observations that might be cited stand as isolated facts, the significance of which can only be surmised in a general way. One of the greatest advances in physiological chemistry in recent years deals with chemical reactions which, by the breakdown of products of intermediary metabolism, release energy to the tissues. At each step in the oxidation of these various substances, energy becomes available through an electronic change; the action is aided by specific hydrogen carriers, aided in turn by enzyme systems to combine ultimately with oxygen. This substance is activated by specific enzyme systems (cytochrome and yellow oxidase). For each step, and for each substrate, special enzymes must be present to act, for without them the metabolic processes cease to be normal or to progress to completion. Considerations such as these suggest that it is in the determination of the kind and distribution of enzymes, or in the local conditions under which these systems work, that the sex hormones govern the several aspects of reproductive function.

Despite the fact that so much of uterine physiology, biochemistry and histology is known, little attention has as yet been paid to this fundamental aspect of gynecic physiology. Until it is, the mechanisms by which the several hormones exert their respective effects will remain obscure. It seems safe to say that the greatest advances in the future in gynecic physiology lie along these lines. With this thought in mind, we therefore turn to the prevalent ideas regarding the nature of the intermediary metabolism and excretion of estrogens and progestogen respectively.

Metabolism of Gynecogens. Interconversion of Estrogens. There are three primary estrogens, estrone, estradiol, and estriol. Of these, estradiol is most potent on injection, and is believed, therefore, by many to be the true follicular hormone. The interrelationship between these native hormones is now so well established that it is perhaps superficial to regard any one as the "true" hormone, when all play a part in the manifestations of estrus. Recent work by Pincus and his associates, which is briefly summarized below, indicates the extent to which this is so.[45,46] The following general facts may now be stated with assurance:

1. Estriol is an end product of estrone and estradiol conversion in the body (rabbit). This is exemplified in part by the fact that when estriol is injected into rabbits in virtually any sexual state (in heat, pregnant, pseudopregnant, hysterectomized in heat, hysterectomized-pseudopregnant, or recently ovariectomized) the urinary estrogen is recoverable as estriol only. It is not modified by ovarian activity or the state of the uterus. The amount of estrogen recoverable in proportion to the amount injected, however, is definitely affected by ovarian activity; thus the percentage recovery is much increased by the presence of progesterone.

2. Estrone is modified when injected into rabbits according to the condition of the reproductive tract. Thus, in rabbits that are in heat, pregnant, or pseudopregnant, both estrone and estriol are recoverable in the urine. After ovariectomy of long standing, or after hysterectomy (with the ovaries present or absent), however, only estrone is excreted upon injection of estrone. It therefore follows that estrone is converted into estriol in the uterus, and for this to take place, the uterus must be under active ovarian control, since several months after castration, conversion does not take place. Regardless of whether estrone or estriol is excreted in the urine, the total estrogen recoverable represents only a fraction of that which is injected; consequently, destruction of estrone as well as of estriol takes place *in vivo*.

3. Regarding destruction of estrogens in the body, it seems certain that the liver is primarily involved. This is suggested by the fact that benzoylation (i.e., esterification) allows almost complete recovery of the hormone in the urine. Moreover, when ovarian transplants which have not been

effective on the mesentery are relocated at a site where the portal circulation is circumvented, they become highly effective.[47]

4. Estradiol is found in only minute amounts in the urine after injection of estrone into rabbits; there is, therefore, little conversion of the ketone into the diol form. After the injection of estradiol, however, estrone is the preponderant hormone excreted, although estriol may be present if the ovaries are in the luteal phase, or if progesterone is injected. This conversion of estradiol to estrone occurs only if functional ovarian tissue is present, and is unaffected by the presence or absence of uterine tissue. The conclusion therefore follows that estradiol, the "true" follicular hormone, is rapidly converted into estrone; this substance is, in turn, partially inactivated by the liver, partially excreted as such, and partially converted into estriol, provided that functional uterine tissue and progesterone are present.

5. Progesterone has important effects upon the metabolism of estrogens, as mentioned above. It increases the quantity of estrogen excreted in the urine, presumably through a sparing action of the estrogens from destruction by the liver enzymes. How this is brought about is not known. Pincus suggests that perhaps progesterone is more readily attacked by the same liver enzymes that inactivate estrogens, so increasing the quantity of the latter hormones available for urinary excretion. It is considered certain that the effect of progesterone is mediated through a sparing action, and not through a change in kidney threshold to estrogens. Progesterone's second action is in the conversion of estrone to estriol, where it acts in conjunction with functional uterine tissue.

The foregoing facts offer a nice explanation for the well known increase in blood and urinary levels of estrogen in the latter (luteal) part of the menstrual cycle. This phenomenon has been heretofore difficult to explain on the basis of an active follicular phase in the first part of the cycle, associated with a low level of estrogen excretion. It now appears that in the early interval there is a different type of estrogen metabolism involving a high degree of estrogen destruction. Estrogen production continues at a high level throughout the menstrual cycle, with increased excretion, as progesterone spares it from destruction by the liver.[48]

Two other aspects of progesterone metabolism in the endometrium deserve mention: it gives rise to glandular growth and permits ovum growth. Together, these include, among other things, mitotic hyperplasia, glycogen deposition, secretion and sensitization of the endometrium for nidation. The effect of the several primary estrogens on each of these endometrial effects of progesterone is not identical.[49] For example, the presence of an excess of estrone, combined with simultaneous administration of progesterone, inhibits both gland growth and ovum growth but it affects the latter response first. Estradiol and estriol, in contrast, inhibit glandular growth without affecting ovum growth directly. "It is a matter of some moment," Pincus and Werthessen write, "that estrone inhibits both egg growth and glandular proliferation, whereas [estradiol and estriol] do not . . . while definitely decreasing the degree of glandular proliferation. It indicates that [estradiol and estriol] are not involved in exactly the same reactions as estrone."

Mechanism of Estrogen Action. A number of considerations of the foregoing sort suggest that in the uterine metabolism of estrogens, a chain, or group, of reaction systems acts upon, or requires the participation of, the hormone molecules. It is supposed[49] that because of this chain of related reactions, many points are available for synthetic substances of suitable configuration to act, and so exert an estrogenic effect from that point in the chain. This theory offers a basis upon which the fact that numerous substances of varying molecular configuration (such as stilbestrol, tetrahydrophenanthrene, etc., etc.) can exert pseudoestrogenic effects of varying

degrees. This is exemplified in the following statement by Pincus and Werthessen: "The vaginal effect presumably occurs at a point in the chain wherein rather wide variation in chemical structure does not necessarily hinder activity. Participation in certain of the uterine reactions on the other hand requires more specific structural configuration; the reactions involving ovum growth, for example, are unaffected by certain native hormones which do affect both uterine proliferation and vaginal activity."

End Products of Progesterone Metabolism. The end products of the metabolism of progesterone in the body are just beginning to be worked out. The situation does not lend itself to brief summary.[2] It is likely that pregnandiol (combined in the liver with glucuronic acid) is the principal urinary end product of such metabolism in the human.[50,51] In general, this substance is present in the urine during the latter part of the menstrual cycle. It is recoverable (about 40 per cent of the theoretical amount) after injection of progesterone in ovariectomized women and normal males.[52] It has also been found in the urine of a male with Addison's disease.[52] Finally, it is present in human urine throughout pregnancy, even after ovariectomy early in pregnancy. This signifies that progesterone is produced in human pregnancy outside the corpora lutea, most probably in the placenta (Venning and Browne).

There is doubt concerning the site at which progesterone is converted into pregnandiol. Some investigators find that after injection of a small amount of progesterone into hysterectomized women (with the ovaries present), no pregnandiol is recoverable in the urine; others find that larger amounts of progesterone given to similar women yield pregnandiol. This has been regarded as indicative of the rôle of the liver in conversion of progesterone to pregnandiol.

There are a number of difficulties encountered in regarding pregnandiol as the sole end-product of progesterone metabolism, even in women. First, some women may excrete pregnandiol in the absence of a well-marked premenstrual endometrium; second, some women with premenstrual endometria may not excrete pregnandiol; and third, pregnandiol is not found in the urine of laboratory animals (rabbit, monkey), even after the injection of progesterone. Since less than half of injected progesterone is recovered in the urine of women, a large share of it remains to be accounted for. The present methods of extraction measure only pregnandiol-glucuronidate and not free pregnandiol or other combined forms, nor do they measure any other end-products which may be present. There are, it is estimated, more than ten probable end products of progesterone metabolism in the body.

Carcinogenesis and Estrogens. One reads with increasing frequency of carcinogenesis as a danger to be recognized in prolonged estrogen therapy. The essential facts in this regard will therefore bear enumeration.

In the first place, it *is* possible to produce carcinomata in mice—but only mice thus far—by injecting estrogen for long periods of time in immature female or mature male mice of strains in which most of the females develop mammary cancer between the ages of six to twelve months.[53] The tumors lead to death within about six weeks after the first appearance of small, palpable nodules. Such tumors induced by estrogens in males are truly carcinomatous, since bits of this tissue transplanted to untreated males grow into tumors which are lethal without further estrogen treatment. In immature females subject to prolonged estrogen treatment, cervical cancer may be produced if the mammary cancer, which invariably appears first, is repeatedly trimmed away. According to Edgar Allen (personal communication), the total quantity of carcinomatous mammary tissue thus removed may appreciably exceed the total weight of the animal itself. Fibromyomata have been produced experimentally in guinea pigs by prolonged (up to

eight months) estrogen therapy, but not in mice, rats, rabbits or monkeys.

To summarize, true carcinomata have only been produced in strains of mice which have a strong genetic susceptibility to carcinoma; without this genetic factor, estrogens have never been shown to be carcinogenic.[53] To date, only mice have proved susceptible to this aspect of estrogen action. Finally, one should note that other factors operate which may predispose toward or against growth of carcinoma resulting from estrogens in susceptible strains of mice. Thus, an essential oil (heptyl aldehyde) added to food decreases the incidence of certain types of malignant tumors in mice.

UTERINE PHYSIOLOGY: SOME RECENT ADVANCES

Uterine Growth Stimuli. Two types of normal growth stimuli are recognized for the uterus: hormones (chemical) and distention (physical).[8] Of the former, estrogens elicit marked hyperplasia of connective tissue elements in the uterus, with subsequent conversion into smooth muscle elements (neogenesis). They have no known effect on mitotic division in smooth muscle fibers, although they bring about extensive hypertrophy of all constituents of the uterus. Estrogen favors extensive mitosis in the epithelium of the endometrium in normal growth and repair.

Progesterone has somewhat different effects, in addition to the well known progestational proliferation of the endometrial glands. It is the hormone par excellence for causing mitotic division of the smooth muscle elements of the myometrium; it does not, however, favor hypertrophy of these tissues. The bearing of the differing predilections of estrogens and of progesterone on connective tissue and smooth muscle in the uterus, respectively, on specific gynecological conditions is not clear. They are facts, however, which may prove useful in future gynecologic studies dealing with the etiology of abnormal uterine growths.

In addition to hormonic stimulation of uterine growth is the second one of uterine distention. The latter has been demonstrated by insertion of pellets of suitable size into uteri of untreated, ovariectomized rabbits.[8] Within four days after such a procedure, marked and characteristic uterine growth effects take place. These include increase in the amount of fluid throughout the entire region of distention, and mitotic hyperplasia and hypertrophy of the myometrium in particular. The effect is not traumatic, for it is devoid of any evidence of leucocytic infiltration.

When distention is combined with estrogens and progesterone, an unexpected change in the growth response takes place. With estrogen, the distention-growth response is absent, and with progesterone, it is diminished by about 50 per cent. The nature of the mechanisms involved in each of these responses[8] and their relation to uterine growth during pregnancy need not be reviewed here. It suffices to point out that, so far as the gynecologist is concerned, the effects of uterine distention (induced by insertion of stem pessaries) on the size of the hypoplastic uterus and on ovarian hypofunction is old knowledge (Dickinson and Smith).

Uterine Cervical Changes. Cyclic fluctuations in uterine cervical secretions have been recognized for some time. Their relation to the transport of spermatozoa through the cervix has only recently been demonstrated.[54,55] Lamarr and his associates have estimated in women during the menstrual cycle the quantity, viscosity, pH, leucocytes, and sperm-penetrability of cervical mucus. They found that the extent to which spermatozoa penetrate this fluid varied with several measurable factors, and that it is limited to a few days in the middle of the cycle. It is at this time that ovulation is believed to occur in women.

During these few days, cervical mucus is most abundant, the pH is highest (up to 7.5), few leucocytes are present, and the viscosity is lowest. In view of current teachings that uterine contractions are not

necessary for, and probably are not a factor in, sperm entry into the uterus,[8] the control (by hormones) of optimal conditions in cervical mucus may be deemed important in the treatment of sterility in women when other sterility factors are absent.

Vaginal Smears. Much is being written in certain journals concerning the usefulness of vaginal smears as a diagnostic aid in the evaluation of hypo-ovarian function, or of the effectiveness of follicular hormone therapy.

Characteristic smear-types may be obtained from the human vagina, not unlike those obtainable from certain laboratory rodents. Papanicolaou, who, with Stockard, discovered vaginal cycles in guinea pigs in 1917, reported[56] this phenomenon in women in 1933. With Shorr, he demonstrated[16] in 1936 its applicability in evaluating the effectiveness of estrogen therapy.

The technique is not difficult to carry out, but it must be meticulously followed for satisfactory results. According to Shorr (personal communication), the failures other clinicians have encountered are attributable to uncritical attempts at simplifying the procedure of obtaining or staining the smears. Saline is admitted to and retrieved from the vagina by a pipette inserted 5 to 6 cm. beyond the vaginal orifice. The fluid is put on a slide, dried, placed in an alcohol-ether mixture, and then successively taken through alcohol dilutions into distilled water. Staining is carried out in successive stages, through Erhlich's hemotoxylin, eosin, and water-blue. The smear is evaluated by judging the amount of mucus, the number of leucocytes, the number of erythrocytes, clearness of the smear, the number of deep and superficial cells, the grouping characteristics of the cells and the number of cornified cells in the smear. For important details of this technique, one should consult the original articles[56,16] since this procedure lends itself readily to office practice with only minor laboratory facilities.

Menstruation Mechanisms. The causes of menstruation are unknown. While it was thought a few years ago that a special "bleeding hormone" of the anterior pituitary was involved, this view is now discredited. The immediate stimulus for menstruation in all probability resides within the uterus. This is shown by the fact that menstruation begins at different times in various parts of the endometrium. Two important questions therefore arise, namely, what local tissue changes precede the onset of menstruation, and by what mechanisms do the several gynecogenic hormones control these changes? The succession of brilliant studies by Markee[57,58] give the answer to the first question, while theories of various investigators[59,8] must suffice, for the present, to answer the second.

A necessary condition for menstruation in monkeys is a period of intense ischemia of the superficial portion of the endometrium. This lasts for some twelve hours and is associated with, or followed by, prominent and characteristic changes in the endometrium. Thus, there is marked thinning of the endometrium, loss of water and increased coiling of the spiral arteries with hemostasis. These changes are followed by leucocytic infiltration of the superficial stroma and subsequent necrosis. The typical papilla, hemorrhage and repair follow.

Among the foregoing local tissue changes, there are two which *must* occur if menstruation is to take place; the blanching is indirect cause of them both. One is that thinning of the endometrium must take place, the other, that spiral arteries be present to give rise to increased coiling of, and hemostasis in, the blood vessels of the superficial stroma.*

The phenomenon of thinning of the endometrium begins late in the blanching (ischemic) period and exhibits important variations. It may take place so slowly that little, if any, bleeding occurs. If thinning is

* The spiral arteries have been described in detail by Daron[60] and by Bartelmez.[59] These structures arise from the vascular zone in the myometrium, pass through the basal zone which is separately supplied by non-spiral vessels.

precipitous and extensive, however, the duration and rate of blood flow will be great. Abnormal manifestations of the former would thus occur as amenorrhea or oligomenorrhea, of the latter as menorrhagia. If the change occurred aperiodically, it would be classed as metrorrhagia.

It is important to note that the *rate* of endometrial thinning is governed by the rate at which the influence of the gynecogenic hormones is withdrawn, while the *extent* of the thinning is determined largely by the thickness which the endometrium has attained during the interval, at the time of uterine growth. We may turn in conclusion, therefore, to the nature of the hormonic conditions which are associated with the onset of menstruation, for on a proper understanding of this will rational therapy of menstrual disorders largely depend.

Menstruation and Hormonic Factors. As mentioned above, the flow of menstrual blood is governed in part by the extent to which the uterus has grown in the interval between menstrual bleedings. This is determined to a great extent by the proper association of hormonic and dietary factors, the first of which have been considered briefly in the first part of this article. What is said below refers more particularly to hormonic factors immediately associated with the onset of menstruation.

Menstruation may be induced in monkeys and in women by a variety of methods.[6,8,59] Thus, it occurs soon after withdrawal of the hormone in a course of estrogen treatment in ovariectomized monkeys or women; it occurs after ovariectomy during a functional cycle (except when the operation is performed on the first day of menstruation); it takes place when the level of estrogen is lowered during a course of injections; and finally, it occurs after the withdrawal of progesterone during a course of injections. The onset of menstruation may be inhibited by other procedures. Thus, progesterone (or testosterone), given immediately following any of the foregoing procedures but the last, inhibits the establishment of menstrual bleeding until the progesterone is withdrawn. Estrogen will delay the menstruation associated with ovariectomy, but not that which follows withdrawal of progesterone. It should be noted once again that the common physiological denominator for all these various conditions is the state of the superficial portion of the endometrium, as mentioned in the preceding section.

There is one important modification in the method of inducing menstruation which Zuckerman[61] and Corner[62] have separately described. They noted that in addition to local conditions within the uterus which are responsible for the blanching, there are also periodic systemic changes of an as yet undefined nature which affect the sensitivity of the uterus to hormonic stimulation. The observation is this: if ovariectomized monkeys are given small, constant amounts of estrogen daily, week in and week out, uterine bleeding occurs periodically. This can only mean, that at such times a change within the system occurs which renders the endometrium unsusceptible (i.e., raises the uterine threshold) to the constant level of estrogen. This would then be functionally comparable to the experimental withdrawal of the gynecogenic hormones, which the earlier experiments in monkeys and in women have merely simulated. Consequently, it appears unlikely that a "cause" for menstruation will ever be discovered; rather, it is more probable that a number of related and interdependent local and systemic conditions will be found indispensable in this phenomenon.

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ENDOCRINOPATHIC AMENORRHEA: CAUSES AND TREATMENT*

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AMENORRHEA refers to the absence of recurring periods of menstrual bleeding at approximately one month intervals. Amenorrhea before the menarche, during pregnancy, and after the menopause is controlled by endocrine forces. When amenorrhea occurs under other conditions it is frequently due to morbid endocrine situations. These include several subtypes, such as (1) delayed menarche; (2) hypoplasia of genitalia; (3) ovarian hypofunction, with or without obesity; (4) postpartum amenorrhea and sterility; (5) premature climacteric. Unfortunately the differentiations between these diagnostic groupings are not as precise as the words suggest. Experience with a large number of women complaining of amenorrhea will be certain to include some instances which might as reasonably be placed in any one of these five categories as in the group mentioned before or after it. In other words, this series of diagnostic terms represents, rather than qualitative differences, merely quantitative variations in the activity of anterior pituitary and ovarian secretions. The exact diagnostic differentiations often involve use of facilities and training which are not at present available to the general practitioner. It may, nevertheless, be of interest to present for general medical readers the diagnostic and therapeutic methods currently in use for the handling of patients with amenorrhea. Most such cases when detected by the general practitioner should be seen in consultation by the gynecologist especially experienced in endocrine work, and should be treated over a period of months by the two in collaboration.

Histories need to be taken in careful detail as to menstrual rhythm and fertility.[1] Physical examinations may reveal many contributory facts about the endocrine status of the woman. But the skillful bimanual pelvic examination is indispensable. If it leaves any uncertainty it should be repeated under simple general anesthesia. At this stage in examination plans should be laid for securing endometrium, either with the curette or one of several types of biopsy instrument. From the microscopic study of this tissue, correlated with the interval since the onset of the last menstrual flow, much can be determined about the nature and intensity of the ovarian hormone secretion. Thus far the methods are available to any physician practicing gynecology. Limitations on the diagnostic study of the endometrium are being obviated by recent reports of the types found under such circumstances,[2] so that competent pathologists can now learn to discriminate types of endocrine action.

In those clinics where special attention is given to this field of endocrine disturbances in gynecology there are several laboratory methods being used increasingly to advantage. One is the study of the stained smear of vaginal mucosal cells.[3] This is not extraordinarily difficult, but interpretation requires some experience not easily put into print, although easily acquired by observation with someone who has this experience. Another method is the assay of urine specimens for pituitary and ovarian hor-

* From the Wisconsin General Hospital. These investigations have been supported by special grants from the Wisconsin Alumni Research Foundation over a period of several years.

mones. The assay methods suffer from lack of sensitivity, paucity of data obtained from normal women, and great cost. Assays must be restricted for some time yet to research clinics.

Accessory technical methods frequently of use are *x*-ray study of the sella turcica region, examination of visual fields for evidence of neoplastic lesions adjacent to the optic chiasm, and basal metabolism measurements. Amenorrhea rarely is associated with a pituitary tumor, but the possibility must be kept in mind until eliminated by the *x*-ray and eye examinations. The Cushing syndrome is striking and not easily overlooked. Basal metabolism determinations are probably misused more frequently than omitted. Unless there is good clinical evidence of hypothyroidism associated with lowered metabolic rate in cases of amenorrhea, it is wise to seek confirmation by the determination of blood cholesterol. Although the *x*-ray and basal metabolic rate are available in every hospital, blood cholesterol is not so widely in use. Where dependable blood chemical work can be done this is worth adding to the repertoire of the laboratory.

DELAYED MENARCHE; PRIMARY AMENORRHEA

In the northern parts of the United States the menarche occurs between 12 and 15 years of age. The average is 14, and, of course, healthy girls occasionally begin menstruating before 12 or after 15. Therefore, it is considered unwise to initiate therapy for delayed menarche until after 15. Exceptions may well occur if there is no sign of adolescence during the 12 to 15 year period, indicating that maturity is much delayed. If the delay in onset of menstruation becomes significant, a careful pelvic examination should be made to determine whether the genitalia and especially the uterus and ovaries are present. Although this seems rudimentary, it is still being omitted. If such examination leaves a question in the mind of the examiner that there may be rudimentary ovaries and a uterus which cannot be felt, a therapeutic test is now possible. The procedure used in this clinic is most easily illustrated by a case.

A girl of nearly 17, who was referred because of primary amenorrhea, had very small breasts but was otherwise a well built, healthy young woman. History and physical examination gave no clues to a cause for amenorrhea. School history, basal metabolism, and blood cholesterol determination agreed in eliminating hypothyroidism. She had been seen by three physicians, none of whom had made a pelvic examination. Under anesthesia no ovaries were palpable, a cervix was seen, but no uterus could be felt, and even with a curette no tissue was obtainable from the very shallow cavity entered through the cervix. Since there was doubt about the existence of ovaries a therapeutic test was undertaken. Daily injection of 100 units of pituitary gonadotropic extract (prephysin) was continued for fifteen days, and repeated after an interval of two weeks. Vaginal epithelial smears obtained before and after this therapy showed no evidence of estrogenic effect. The cells were of the type characteristic of the deeper layers of vaginal mucosa. The conclusion drawn was that if ovaries were present in this girl, they were rudimentary, and the prognosis for establishing the menses was considered extremely dubious. No further therapy was advised. It is obvious that such a prognosis could not be expressed with any confidence unless there had been previous experience with the same gonadotropic extract to justify confidence in its potency. The next case will illustrate this.

A woman of 25 was admitted to the psychiatric service because of numerous personality problems, including her fear that she was "turning into a man." The family and referring physician believed permanent institutional care necessary. The history of primary amenorrhea led to a suggestion of endocrine study. The patient refused to allow a pelvic examination, even by a woman. Vaginal smears were obtained, and were typical of castrate mucosa. Thereupon she was given 100 unit doses of prephysin daily for fifteen days. After two days estrogenic activity was in evidence, and a marked change had appeared after ten days. Four days following the interruption of this therapy her first menstrual flow began and con-

tinued for seven days. These events indicated that she had ovarian and uterine tissues, and that the gonadotropic extract was potent. Another course of therapy caused a second flow three weeks later. During the following eight months she received six further series of treatments. No flow occurred, although she made striking psychologic improvement, and was able to leave the hospital after the first flow. The vaginal smears continued to show moderate estrogenic activity, and a curettage obtained ten months after the first therapy showed low intensity of glandular growth, with some areas of cystic glandular hyperplasia. The uterus was obviously small. Two brief menstrual flows occurred within the following month, but during the next twenty-six months, in spite of persistent use of cycles of treatment, no further flows have been observed. On four occasions treatments have been interrupted and each time there has been gradual relapse of the psychic status, followed by a good recovery when therapy was resumed. Vaginal smears have continued to indicate estrogenic response to the use of prephysin, and similarly to the gonadotropic (maturity) extract of Armour or of Ayerst, McKenna and Harrison, and to pregnant mare serum concentrate, gonadin, of the Cutter Laboratory. It will probably never be possible to stimulate the ovaries in this woman to the point of fertility, but sustained treatment has served to rehabilitate her psychologically and economically, which is justification for its continuance.

The prognosis in primary amenorrhea is poor if pituitary secretion is so low that one must supply all the gonadotropic stimulation hypodermically, and if the gonads are infantile. Perhaps better forms of gonadotropic therapy will become available.

HYPOPLASIA OF GENITALIA

The cases of primary amenorrhea cited above have had poorly developed internal and external genitalia. Similar hypoplasia may be associated with secondary amenorrhea, with infrequent, scanty, irregular menses, or with menorrhagia. These are probably various manifestations of the same underlying hypofunction of pituitary and ovaries as previously described.[4] One special case is that of the woman whose amenorrhea is complicated by asthenia, loss of weight, hypotension, and numerous nervous complaints. It is in such patients that one finds difficulty in deciding between anorexia nervosa and Simmonds' cachexia. The onset is usually insidious. There are seldom anatomic findings which indicate pituitary involvement. Occasionally the psychologic problem is obvious, more often it requires patient search to find why the woman will not or cannot eat an adequate diet to maintain normal weight. Detailed study of several such patients has failed to reveal evidence for hypothyroidism or adrenal deficiency, or for chronic infection.

Endometrium is usually scanty, with few glands, and no evidences of progestational changes. Vaginal mucous membrane is not of the castrate type, but shows less cornified cells than expected for the age of the woman. The menstrual flow has often been absent for many months or several years. Use of potent gonadotropic extracts in large doses repeated for several consecutive months has been surprisingly futile in this type of patient. Intensity of estrogenic response has not increased, judged by vaginal smears, endometrial biopsies, occurrence of flows, or subjective changes. It appears that these women are not without ovarian activity, but that for some reason their ovaries fail to respond.

In a few cases we have been able to demonstrate in the urine of such women as much gonadotropic hormone as is found by the same technique in young women with regular menstrual cycles. We, therefore, incline to group these patients as anorexia nervosa, and to attribute the amenorrhea and hypoplasia to prolonged undernutrition. That this is not an entirely satisfactory explanation is suggested by the fact that severe undernutrition of large portions of the population because of economic stringency has not usually produced amenorrhea. Probably there is a combination of undernutrition and some other inherent individual factor leading to the genital hypoplasia and asthenic state. To date no

success has attended endocrine therapy in this condition.

HYPOFUNCTION OF OVARIES

Secondary amenorrhea may occur with grossly normal genitalia, including a well developed uterus. If this hypofunction is associated with obesity, it constitutes one type of the Fröhlich syndrome. The obesity is by no means essential, and when overweight is a problem it must be treated by dietary restriction and increased exercise as in any other patient. The prognosis in such cases is often good if gonadotropic therapy is used.

A woman of 19 was referred because of amenorrhea for six months, and sterility since marriage at 16. Menses had begun at age 12; the duration of flow had gradually declined from three days to complete absence of bleeding, but leucorrhea was present. Moderate obesity had developed slowly. There were few symptoms resembling the climacteric. Basal metabolic rate was plus 18. Pelvic examination was in no way remarkable. Endometrium was easily obtained with a biopsy punch, but showed very little activity, no mitotic figures, and a dense stroma. The patient began use of prephysin in 100 unit doses daily for fifteen days, and was sent home. Menstruation did not occur. She had been told to repeat the series of injections beginning with onset of the next flow. or after a month if no flow appeared. After three months her referring physician reported her probably pregnant, and her delivery occurred nine months after the only series of gonadotropic injections. Lactation was satisfactory.

The restored fertility in this patient seemed surprising, but similarly prompt response to therapy has occurred in several women. It cannot be expected as the rule. More frequently repetition of the treatments at monthly intervals appears necessary. If regularity of rhythm shows improvement, if vaginal smears show increasing evidence of estrogen action, if symptomatic improvement is definite, gonadotropic therapy may well be repeated at monthly intervals for several years. Since the cyclic activity of the ovaries increases beginning at about the time of onset of a menstrual flow, we choose this date as the most appropriate one for resuming the successive series of hypodermic injections. We have consistently avoided using continuous daily treatment, to prevent developing cystic ovaries. Instead we have employed from five to fifteen doses, distributed over five to fifteen days of the cycle. If flows do not recur at intervals of at least six weeks, we feel justified in resuming therapy without longer intervals.

Amenorrhea and other evidences of hypofunction of pituitary and ovaries may depend on secondarily depressed action due to hypothyroidism or adrenal insufficiency. Examples will illustrate the way in which pituitary gonadotropic therapy may help even such cases.

A student, aged 20, was examined because of change from her usual four week cycles to the occurrence of only two menstrual flows in thirteen months. She was at least 35 per cent overweight, had a basal metabolism of minus 14, and pelvic examination showed a small and retroverted uterus. Endometrium, obtained ten weeks after the last flow, resembled that found after castration. It was felt that the diagnosis was more probably the Fröhlich syndrome than hypothyroidism. Use of gonadotropic injections, 25 units of prephysin, led to resumption of menses. The number of doses was increased to five daily doses followed by five on alternate days, beginning at the onset of each flow. Improvement was evident from the first, and after eighteen months cycles were substantially regular of the four weeks type. Following twenty-six months' therapy the gonadotropic injections were stopped, and cycles have continued very dependably regular. Weight control was not facilitated, and, therefore, after six months without treatment the use of thyroid was begun and has been continued with better weight control, as well as with slightly shorter and more uniform duration of flow.

In considering the responses of such a patient it is impossible to determine whether the primary fault was hypothyroidism or hypopituitarism. It has been

noted in animal experiments that if thyroid function is depressed, the anterior pituitary shows cytologic alterations[5] which might easily be responsible for such alteration of function as this patient showed. The Fröhlich syndrome is not usually accompanied by evidences of hypothyroidism, but it is possible that at times the decreased function of the pituitary may affect the gonads and also the thyroid. In practice it is probably wise to use thyroid therapy as the first approach only if and when there is good clinical evidence of thyroid deficiency. If success is not achieved gonadotropic therapy may be added. Similar reasoning applies to the less frequent adrenal insufficiency, or mild Addison's disease. The effects of long continued adrenal insufficiency are illustrated by the following case:

A woman, aged 34, had considered herself well until the previous four years, during which interval she had several attacks marked by vertigo, nausea, and hypotension. Complaints included fatigue from slight exertion, weakness, tremors, backaches, scotomata, paresthesias, palpitation, and constipation. Menstruation began at 14, had been of a regular four week type, but with gradual decrease in duration of flow from age 20 until amenorrhea occurred at age 31 after the symptoms became markedly severe. A miscarriage occurred at age 21, after which no further conception had been possible. When first seen at age 34, she was in a remission of the Addison's disease, which was still demonstrable by studies of blood volume and serum sodium response to salt restriction. Menses were recurring but at intervals of three to five weeks. Endometrial biopsy showed a progestational reaction, which was characterized as degenerative in appearance. Following a period of some two years use of added salt and potent adrenal cortex extract, menses were restored to a regular four week rhythm of four to five days flow. Fertility has not been restored. This woman is believed to have had a long-standing adrenal deficiency, probably of the atrophic rather than the tuberculous type. The depressing effect on ovarian function is parallel to the general asthenic picture, and both have shown good response to adrenal therapy, without use of either estrogen or gonadotropic hormone.

POSTPARTUM AMENORRHEA AND STERILITY

The reports of Sheehan[6] have called attention to the probable mechanism involved in the irregularities of menstruation, amenorrhea, and loss of fertility which not infrequently follow pregnancy. As with other lesions, there are quantitative variations in the extent of the disturbance produced. Examples will illustrate the varied prognosis depending on the extent of the depression in endocrine function.

A woman of 33 years had one child born two years before, after which her menses were no longer of the regular monthly type, but occurred at approximately three month intervals, associated as never before with prolonged dysmenorrhea. Fertility was reduced. Obesity, acne, abdominal pains, as well as hot flashes, sweating attacks, dyspnea, headaches, weeping, worrying, paresthesias, and self-depreciation had appeared after the puerperium. Physical findings were not remarkable aside from moderate obesity, which was controlled by diet, and blood pressure 138/110. Pelvic examination discovered bilateral moderate enlargement of the ovaries, and retroversion of the uterus, which was corrected by a pessary. The endometrium obtained on the twenty-eighth day of a fifty-two day cycle was not typical of any stage in the normal cycle. Estrogenic activity was apparent but of varying and low intensity, with some mitotic figures seen. It was felt that the differential diagnosis lay between premature menopause and postpartum hypopituitarism. Due to the early age and the desire for further children, an effort was made to stimulate the ovaries by the use of pregnant mare's serum concentrate (gonadogen), given ten units hypodermically on alternate days. After a total of twelve such doses, in three cycles, with three menstrual flows occurring at intervals of four and seven weeks, the patient became pregnant and went to term. She was given progesterone as a measure of safety during the first trimester. Subsequent to the second pregnancy menses were again irregular and infrequent. Menorrhagia led to hysterectomy, at which time cystic ovaries were found and removed, but the symptoms suggestive of the climacteric have no longer been evident.

The favorable outcome of this case is to be contrasted with the persistent difficulty in a 24 year old woman after birth of a child at age 19. Delivery was followed by a syndrome resembling surgical shock. Menses were always irregular after that, and ultimately led to amenorrhea at age 23. Other symptoms were occasional hot flashes, marked asthenia, weeping, morbid worrying, insomnia, and self-depreciation. The breasts were almost constantly painful, and some swelling was noted. Blood pressure was 90/60, basal metabolism minus 13 per cent. Under anesthesia the uterus was found to be distinctly small, and endometrium was obtained with difficulty with the curette, the tissue appearing typical of the castrate. Vaginal epithelium obtained by the smear technique showed very slight estrogenic activity. The patient was started on a program of pituitary gonadotropic injections, using 100 units of prephysin daily for ten doses. Vaginal smears showed a slight, but distinct response, which was not progressive. After three such courses of treatment in three months the vaginal response was not improved and no flow appeared. There was no significant symptomatic change. It was, therefore, concluded that the extent of pituitary failure was so profound that the amount of therapy necessary to reëstablish menses and fertility would be impractically large. It was advised that treatment should be limited to sufficient amounts of estrogen to relieve symptoms.

PREMATURE MENOPAUSE

There is difficulty in distinguishing between the last case and the occasional spontaneous cessation of menses earlier than the middle of the fifth decade. It is assumed that the menopause refers to cessation of ovarian secretion of hormones because of inability of the ovaries to respond to gonadotropic stimulation.[7] The gonadotropic secretion of the pituitary is probably increased at and after the climacteric, judged by microscopic appearance of the anterior lobe,[8] by gonadotropic hormone content of the human gland in older women, and by the sustained high gonadotropic hormone excretion in the urine of women during and after the menopause.[9] When the failure of menses is due to pituitary failure as in the two cases cited above, we incline to exclude them from the premature menopause group. By contrast we would place the next patient in this latter diagnostic classification. We hope that assays of urine gonadotropic hormone output will assist in this separation. Preliminary findings indicate that when this hormone output is higher than during the usual fertile period of the third and fourth decades it is probable the ovaries cannot longer respond to gonadotropic stimulation. Such a conclusion will require more extensive validation before it will be dependable.

A woman, aged 35, was referred because of sterility. She was in excellent health and symptom-free, but her usually regular menses had been interrupted for five months. Vaginal smears were examined at intervals of a few days for three months. There were slight fluctuations in estrogenic activity, and menstrual flows occurred at intervals varying from three to six weeks. The use of gonadogen was begun, first with six doses of 10 units each during the first two weeks after each flow began, later with 20 units per dose and as much as 300 units per cycle of therapy. There were occasionally spurts of encouraging increase in estrogenic response shown in the vaginal smears. During one such cycle chemical determination of pregnandiol in twenty-four-hour urine specimens[10] showed the output of 45 mg. in seven days, indicating that ovulation had occurred. Nevertheless, there were only four flows in the succeeding year, and none in the year following. Attempts to induce ovulation during periods of amenorrhea by combining hypodermic administration of gonadogen with intravenous injection of 50 to 60 units after two weeks of such stimulation were futile. No pregnandiol was excreted. Flow did not follow within two weeks. Therefore, treatment was discontinued because it was felt that the ovaries in this woman had become so refractory to stimulation that their period of activity was essentially over. Increased supply of gonadotropic hormone by injection produced too little response to justify continued therapy. This situation constitutes a premature menopause.

In the patient just described there were no climacteric symptoms, in spite of the

very low estrogenic hormone production by the ovaries. The same statement applies to many women at the usual climacteric age. On the other hand, we have seen women as young as 20 in whom premature climacteric symptoms have appeared in violently disturbing intensity, associated with postpartum amenorrhea. It is apparent from these observations and from more recent urinary assays[9] that the occurrence of climacteric symptoms is independent of the pituitary gonadotropic hormone production in menopause states.

THE MENOPAUSE

After the menopause, fertility is not desired, and it is obvious that there is no value to be gained by stimulating the ovaries. If unpleasant symptoms are present, the amenorrhea is to be ignored, and the patient treated symptomatically. Usually this requires the administration of an estrogenic substance. If estrin is given in sufficient doses, and with brief periods of interruption, menstrual flows can be reëstablished. Such flows are of interest in arriving at an understanding of the mechanism of menstruation, but from the patient's point of view the production of a flow is merely a nuisance. It can be avoided by the use of minimal doses of estrogen administered at regular short intervals, rather than large doses given less frequently. The necessary duration of such therapy may be from a few weeks to a few years. Since it can be done simply, safely and economically by oral administration of estrogens, this is at once the commonest and simplest of all types of treatment for "amenorrhea." Of course, the reason for treatment is not the amenorrhea, but the symptoms.

It is possible to treat these same symptoms similarly when associated with menstrual irregularities during the earlier decades. There is far less prospect of reëstablishing menstrual regularity and fertility than if gonadotropic therapy is employed. For this reason we continue to urge that estrogenic hormone be used chiefly for relief of climacteric symptoms, when there is no intent to restore fertile and regular menstrual rhythm.

ENDOCRINE MATERIALS

Our earliest and most extensive experience has been with prephysin, the commercial product, by the Chappel Laboratory, of the extract from the horse pituitary, originally described by our former colleagues, Hisaw and Fevold.[11] This is available in two concentrations, containing 25 or 100 units per c.c., distributed now by the Harvey Company. The disadvantage of prephysin is that it usually causes local inflammatory reactions, due to the protein materials present. A more limited use of the maturity or gonadotropic extract of the Armour or Ayerst, McKenna and Harrison Laboratories has convinced us of its dependable activity. The inflammatory reactions are not so marked as with prephysin, but this advantage is counterbalanced by the lower potency of the material. The unit employed for this material is very much smaller than for prephysin. We have been gratified by the results from pregnant mare's serum concentrate. This has been used in two forms: gonadogen from the Upjohn Laboratory is dispensed in dry tablets, in sterile vials, with saline for solution at the time of injection; gonadin from the Cutter Laboratory is in aqueous solution, and must therefore be refrigerated when not used promptly. These materials cause little or no local inflammatory reaction. In our experience there has been no important allergic reaction to gonadogen or gonadin, and very little to prephysin. We prefer to avoid the use of the concentrates of human pregnancy urine in the treatment of amenorrhea, for this gonadotropic material does not stimulate follicular activity.

For generous supplies of the five gonadotropic extracts described we are indebted to the manufacturers who have thereby made possible the study of an extensive series of patients.

SUMMARY

Amenorrhea may result from failure of the ovaries to respond to pituitary gonadotropic stimulation, or from deficient pituitary secretion. Ovarian failure is characteristic of the menopause, and is to be treated for symptomatic control only, and by the use of estrogenic substances. Pituitary inadequacy may be substituted for by gonadotropic substances obtained from animal pituitary or from serum of pregnant mares. Hypodermic injections of these extracts are advised in series of five to fifteen doses, during the first two weeks of the menstrual cycle, or at intervals beginning not oftener than every four weeks, to attempt reëstablishment of cyclic flowing. Determination of the ability of the ovaries to respond is facilitated by the use of vaginal smears showing the estrogenic effects on vaginal mucosa.

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DIAGNOSIS AND TREATMENT OF FUNCTIONAL UTERINE BLEEDING*

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As the term "functional" uterine bleeding would indicate, our concept of this disorder is that it is due to a functional derangement rather than to a structural lesion of one or other of the organs and tissues concerned in the menstrual cycle. The organs immediately concerned are the ovaries and the uterus, but beyond these, as we know, we must consider the possible rôle of distantly situated endocrine glands, especially the pituitary. As a matter of fact, most of what we have in recent years learned regarding the physiology of menstruation pertains to its endocrinology, so that it is not strange that in the explanation of abnormal menstrual bleeding it is the endocrine factors which have been most stressed.

And yet there is no doubt that functional bleeding is often due, in part at least, to derangements of other cogs in the menstrual mechanism. For example, we know very little as yet about the rôle of the uterine musculature, though it may be important. The perivascular interlacing arrangement of the uterine muscle makes it easy to understand that the degree of contraction or relaxation of these muscle bundles may have much to do with regulating the duration and amount of menstrual bleeding. However, it may well be that behind these variations lie variations in the quantitative balance between estrogen and progesterone, both of which have physiologic effects upon the uterine muscle.

Again, we must remember that menstruation is at bottom a vascular phenomenon, and that the rôle of the spiral arterioles of the endometrium, and probably of the vasomotor nerves, is an important one. The fundamental rôle of the spiral arterioles has been beautifully demonstrated by the experimental studies of Markes upon endometrium transplanted to the anterior chamber of the eye, but here again the endocrine forces probably play the underlying rôle.

I mention these things merely to emphasize that we must not center our attention too exclusively upon the endometrium as a registering board of the endocrine dysfunctions which may bring about functional bleeding, important though such studies are. Not so many years ago it was the myometrium which was the cynosure of study in the attempt to explain "idiopathic" bleeding, and we may still be obliged to take a page from the book of Theilhaber and others, who in those days so valiantly championed the doctrine of "insufficientia uteri" or muscle inadequacy of the uterus as a cause of this type of bleeding. The broad viewpoint, in other words, must include a consideration of all the links of the menstrual chain in the attempt to explain bleeding of this functional type.

The criticism may properly be made that we have tried to fit all cases of functional bleeding into the same dysfunctional mould. In a large proportion, it is true, the underlying disturbance seems to be a failure of ovulation, and a persistence of unruptured follicles beyond the normal span. The endometrium is therefore subjected to an abnormally persistent and excessive estrogenic growth influence, which in at least a considerable proportion of cases, is expressed in the histologic pattern which we call hyperplasia. The latter, it should be emphasized, is not the cause of abnormal bleeding, representing

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only an abnormal growth picture in the endometrium.

As a result of the see-saw functional relationship between the anterior pituitary lobe and the ovaries, periodic drops in the estrogen level occur in such a disorder, with an alternation of bleeding and non-bleeding phases. Since the corpus luteum is lacking in such cases, the characteristic of the endometrium is an absence of the secretory phenomena dependent upon progesterone, but not necessarily the presence of a hyperplasia of the full-blown, so-called Swiss-cheese pattern. There appears to be no parallel between the growth and bleeding propensities of the endometrium, so that in this group of cases one may find a genuine hyperplasia, or an endometrium corresponding to the earlier stages of the normal interval, or even an endometrium of rather atrophic type. Characteristically, however, one does not find secretory changes if the bleeding is due to the mechanism above described, as it is in the largest number of cases.

The fact remains that in a considerable group one may find an apparently normal type of endometrial cycle, with the normal sequence of proliferative and secretory phases. It is in this group that one must invoke other causal factors, such as a quantitative imbalance between the two ovarian hormones, or a disturbance in the spiral arteriolar apparatus, the vasomotor nerves, or uterine musculature. Concerning these factors, however, we know very little, and we are certainly still ignorant as to the nature of the liaison which must exist between them and the ovarian hormones. While, therefore, all these factors and many others must be considered in the explanation of functional bleeding, we must await further investigations before we can discuss all the possible mechanisms intelligently.

DIAGNOSIS

Speaking generally, the diagnosis of the functional nature of bleeding is justified when thorough examination permits us to eliminate all evidence of structural or anatomic abnormalities in any of the pelvic organs. In the frequent bleeding of puberty and adolescence, for example, the functional nature may be assumed when the pelvic organs, on rectal examination, are apparently normal, with no evidence of the rather rare pathologic lesions, such as ovarian neoplasms, which may occasionally be found at this epoch. Few mistakes will be made by this simple method of elimination.

During the reproductive period, however, it is obvious that more direct evidence is necessary, because of the great frequency of intra-uterine pathology, such as retention of gestational products, polyp, submucous myoma, and carcinoma. Not only must extra-uterine lesions be eliminated by careful pelvic examination, but diagnostic curettage must ordinarily be done to eliminate intra-uterine disease. If microscopic examination shows no evidence of chronic endometritis, malignancy or other such lesions, and if there is no suggestion of such lesions as submucous myoma, one is justified in assuming that the bleeding is of functional nature.

The pathologic report on the endometrium in such cases is quite sure to be "normal endometrium" or "benign hyperplasia of the endometrium." If the former, the endometrium will most often be of the proliferative, non-secretory type, but it may be of a secretory variety, as I have already mentioned. If the report is of hyperplasia, the endometrium may grossly be enormously overgrown and polypoid, or it may be of moderate or even scanty amount. Similarly the hyperplasia may microscopically be of the frank Swiss-cheese pattern, or it may show only a moderate degree of hyperplasia. In these age epochs, therefore, the diagnosis is based upon the elimination of definite pathologic lesions, reinforced by the evidence of microscopic examination of the endometrium.

TREATMENT

Aside from certain general measures which are more or less obvious, such as the treatment of the frequently associated secondary anemia, the treatment of functional uterine bleeding must depend upon two chief considerations, namely, the age of the patient and the importance or unimportance of preserving the reproductive function. Another important consideration which must always be borne in mind, especially in the treatment of young patients, is that the ovarian dysfunction responsible for the menstrual disorder is often a temporary one, and that there is a strong tendency in the majority of patients toward a reëstablishment of the endocrine balance, after a bleeding career of variable and unpredictable duration.

It should be remembered, first of all, that the mechanism in most cases, especially those of the pubertal and adolescent type, is only an exaggeration of the anovulatory cycle so common at these periods of life. In other words, many young girls do not ovulate until they have menstruated for many months, or even several years, after menstruation has appeared. In such cases, menstruation may be essentially normal in amount and rhythm, but it may be irregular and profuse. Frequently the adjustment to normal periods takes place without any treatment at all, but, if bleeding is very profuse, the patient presents herself for medical care, and is promptly and properly diagnosed as having functional bleeding.

Bleeding may be so profuse as to necessitate transfusion, sometimes repeatedly. Curettage is rarely necessary for diagnosis, but is often indicated for its value in the immediate control of the bleeding. In cases of this group, as well as in those of older women in whom the desire for future childbearing is an extremely important consideration, we have our chief field for organotherapy. Radiologists as well as gynecologists agree that radiotherapy should be used only as a last resort, even in carefully adjusted small dosage. In my experience such treatment has been necessary in only a very small proportion of cases.

Three chief groups of endocrine preparations are available for the organotherapy of functional bleeding, viz., (1) the pregnancy urine or A.P.L. substances, or, as we now consider them, the chorionic hormone preparations; (2) the progesterone preparations; and (3) the preparations of testosterone propionate.

The pregnancy urine preparations were first employed in the hope that they might bring about luteinization and progesterone production in the human. It should be remembered that when their use was first begun progesterone was not available for clinical use. While it is now known that these substances do not in humans bring about the hoped-for ovarian luteinization, the fact remains that in at least a proportion of the cases they do bring about cessation or lessening of the bleeding, so that they are still widely employed, sometimes with benefit, but often with disappointing results. When they are to be used, an average dosage varies between 200 and 500 units daily during the bleeding phases, though some use much larger doses.

When progesterone became available, it was but natural that it should have been resorted to in the treatment of a disorder in which absence of progesterone seems to be the outstanding endocrine defect. The results present about the same variations as with the pregnancy urine preparations, with sometimes striking effects on the bleeding, but in many instances little or no effect. The dosage has generally been far less than that known to be necessary for luteinization of a proliferative endometrium (60 to 90 rabbit units), varying ordinarily from 1 to 5 rabbit units (mg.) daily. The cost of higher dosage would be prohibitive to many patients. The smaller doses are perhaps not so illogical as they seem, for there is much reason to believe that the bleeding factor in the endometrium, whatever it is, is susceptible to much smaller hormonal doses than those required for its histologic transformation.

Finally, within the past two years or so, the androgenic hormone substances, chiefly in the form of preparations of testosterone propionate, have become very popular in the treatment of functional bleeding. There is still some uncertainty as to the effect of testosterone on the female genital cycle, but the evidence now available indicates that it exerts an inhibitory effect upon follicle ripening and the production of estrogen. Curiously enough, Hartman has shown that when given in the late secretory stage, it produces an accentuation of the progesterone effect.

When used in the treatment of functional bleeding of a periodic or menorrhagic type, testosterone should be given throughout the cycle rather than only after the onset of the bleeding. In milder forms of bleeding, even small doses of perhaps 10 mg. two or three times a week, are often highly effective. In the more severe types of bleeding large doses are required, though I rarely use more than 25 mg. three times a week.

Enthusiasm in the use of this preparation in women has been somewhat dampened by the publication of several cases in which such unpleasant sequelae as hirsutism and even voice changes have developed following this plan of treatment. In the moderate doses which I have employed in a rather large number of cases, I have observed no such effects. The fact remains, however, that if further experience should show that such unpleasant manifestations do occur with any frequency, most of us would be very circumspect in advising this plan of treatment even though these sequelae are of transitory nature. In the meantime I would advise the use of moderate dosage, rather than the large amounts which some have employed.

Finally, functional bleeding occurs most frequently of all in women of the menopausal age, using this adjective broadly as applying chiefly to the fifth decade of life. It is at this age period that more than one-half of all cases are observed. In this large group the indications for treatment are quite different from those applying in younger patients.

Women of middle age have lived their reproductive lives, and the question of further child-bearing is usually of no importance. Their one desire is to be rid of the troublesome bleeding, and they are prepared for the menopause. Why bother such a woman with the uncertainties and annoyances of organotherapy when the problem can be so promptly and effectively solved by the abolition of ovarian function, as can be accomplished in all cases by adequate dosage of radiotherapy? This, therefore, is the rational plan to follow, and it represents one of the most valuable contributions of radiology in the field of gynecology. The use of radium or the *x*-ray for this purpose, however, should never be resorted to until the functional nature of the bleeding is established and other perhaps more serious causes eliminated by diagnostic curettage.

SUMMARY

There are certain cases of functional bleeding in which spontaneous readjustment of the endocrine balance takes place, with reëstablishment of normal menstruation. When the bleeding is sufficiently profuse to impel the patient to seek medical advice, the proper management will depend chiefly upon the age of the patient and the importance of preserving the childbearing function. In young patients organotherapy will usually tide the individual over until the hoped for endocrine readjustment takes place, though curettage may be necessary for the immediate effect. In women of middle age in whom childbearing is no longer a consideration, the treatment in most cases should be diagnostic curettage to eliminate more serious lesions, followed by radiotherapeutic induction of the menopause.

THE TREATMENT OF PRIMARY AMENORRHEA*

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WHEN the menstrual flow has not made its appearance at the average age of puberty we speak of primary amenorrhea. Strictly defined, primary amenorrhea is presumptive evidence of a deficiency in the prepuberty sex impulse of the anterior pituitary gland. This deficiency may vary in degree from being nearly complete to just below the normal.

ETIOLOGY

Physiologists generally agree that menstrual function depends upon the presence of a normally functioning anterior pituitary, a normally developed ovary capable of responding to the anterior pituitary gonadotropic hormones, and a normal uterus which reacts to the ovarian hormones, estrin and progestin. It is obvious therefore that primary amenorrhea may result from congenital deficiencies or from unfavorable conditions arising during the prepubertal period which adversely affect the anterior pituitary, the ovaries or the uterus.

Although the initiation and maintenance of ovarian function is chiefly dependent upon the pituitary, the development of the sexual organs and the appearance of the menstrual flow may be retarded by structural or functional deficiencies in other members of the endocrine system. While the thyroid, the adrenals, the pancreas and other ductless glands are primarily concerned with vital metabolic processes, there is evidence to show that the anterior pituitary gland reflects alterations in their functional status. It follows therefore that disturbances in one or more of these glands may unfavorably affect ovarian function by way of the pituitary.

Non-endocrine factors also may depress the organism as a whole and adversely affect pituitary and ovarian function. Among them are the constitutional and the general diseases of childhood, and the nutritional faults resulting from environment and diet. These remote but important causes have been somewhat obscured by the more spectacular revelations of the past decade which have focussed attention upon the endocrine glands. Although the glands that immediately control gonadal function undoubtedly play the leading rôle, it is equally true that any non-endocrine abnormality which unfavorably affects the general health of the individual may be reflected ultimately in the gonads.

PROGNOSIS

The outlook in an individual case of primary amenorrhea depends not only upon the nature of the underlying abnormality but also upon its severity.

The general appearance of the patient gives some estimate of the difficulties that lie ahead. The prognosis is usually poor in the primary amenorrhea associated with retardation of the primary and secondary sex characters, for in such cases either congenital or developmental defects, or some prepubertal endocrinopathy are usually at fault. When, on the other hand, the condition is associated with normally developed sex characters, menstrual function may be spontaneously established or respond to treatment sooner or later.

Although pituitary insufficiency often involves both its sex and its growth-stimulating functions, exceptionally either one may be implicated alone. Consequently, normal or nearly normal growth

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may be associated with marked depression of gonadal function, difficult or impossible to influence, while, conversely, abnormalities of growth may coëxist with normal or only slightly retarded sexual development which may be quite amenable to treatment.

An important aid in determining the prognosis is a study of the prolan and the estrin in the blood and urine. The presence of an increased amount of prolan, if associated with an absence of estrin is an unfavorable sign, for it may signify an inherent defect in the ovaries which renders them refractory to stimulation. Where no increase in prolan is demonstrable, the outlook is more or less favorable, depending on the amount of estrin present. If even small amounts can be detected, the outlook is fairly hopeful, for it indicates some degree of pituitary activity and the presence of a responsive ovary.

Where both the prolan and the estrin tests are negative, it may be inferred that pituitary function is deficient. Whether in such cases the ovary is likewise inherently defective is difficult to ascertain.

A therapeutic test recommended by Hamblen involves the administration of a total of 3,600 mouse units of pregnant mare's serum over a period of four to six weeks. If at the end of treatment the uterine mucosa fails to show evidence of stimulation by one or both of the ovarian hormones it may be assumed that the ovaries are refractory. This test obviously presupposes the existence of a preparation capable of stimulating the human ovary.

It may be truthfully said that if we are able to remove handicaps to the general health and promote the well-being of the patient, as she grows older endocrine influences that have been dormant may be aroused and our purpose will be achieved.

DIAGNOSIS

Since there is such a multiplicity of influences which may underlie pituitary and genital dysfunction, there is scarcely any problem in the practice of medicine that requires more painstaking and thorough study.

We note at the outset the gross evidence of endocrine disorders. Sometimes the endocrinopathy is stamped unmistakably upon the patient, as for example in cretinism, Fröhlich's syndrome or hypophyseal infantilism. But very often the gross evidence of pituitary, ovarian, thyroid, or adrenal dysfunction may be no more than suggestive and there may be such a combination of evidences that the clinical picture seems hopelessly confused and the predominating influence is a matter of speculation. Particular attention should be directed to the development of the primary and the secondary sex characters and the presence of statural anomalies or other endocrinopathic stigmata.

There are also special studies such as: anthropometric measurements to show the relative proportion of growth and sex impulses; basal metabolic estimations to measure the influence of the thyroid; sugar tolerance tests which may furnish some clue to the functional status of the pituitary; mapping the visual fields, and *x*-ray of the sella turcica to show the probable size of the pituitary gland and to disclose any sign of tumors of the gland or its environs; *x*-ray of the epiphyses to confirm the external evidence of too little or too much growth as well as the relative proportion between the growth and the sex impulses.

All of these procedures are preliminary to an actual study of the ovarian and the pituitary hormones in the blood and urine of which we have already spoken. In the normal case the ovarian hormone, estrin, is scarcely appreciable at the beginning of a cycle but gradually increases toward the end, the optimum time for its recognition being just before a period is due. In the primarily amenorrheic we have no basis for selection of this time. If no ovarian or pituitary hormones are discovered at the first examination or if the estimation is inconclusive, then weekly studies of the blood and quantitative estimations of

the total amount of estrin excreted in the urine over the full course of time usually occupied with a menstrual cycle will be needed. Only after such a search could one be certain that the reaction was completely negative. If the result is negative the studies should be repeated from time to time as the individual grows older since there may be a change in the endocrine function either naturally or as the result of treatment.

As no investigation may be considered complete without eliminating the possible non-endocrine causes, a thorough physical and pelvic examination as well as routine laboratory studies are of the utmost importance.

In the young amenorrhoeic no more of a pelvic examination should be made than is necessary to be sure that there are no gross pelvic anomalies. The development of the external genitalia, the distribution of the pubic hair and the size and form of the breasts are appreciable at a glance. The vaginal vault and cervix may be inspected with a Kelly cystoscopic speculum, the patient being in the knee-chest position. Bimanual palpation of the pelvic organs with a finger in the rectum will enable us to form some estimate of the development of the uterus and the ovaries. There is no use, however, in a searching pelvic examination at the beginning of the studies; it entails discomfort and may be otherwise objectionable in the conscious patient. Furthermore the palpable size and form of the pelvic organs may not give us a true estimate of their functional capacities. We find this out with greater accuracy at first by the estimate of hormones in the blood and urine and later by endometrial biopsy.

In obstinate cases we may examine the patient under anesthesia when close palpation of the adnexa is much facilitated. Exploration of the uterine cavity, curettage and hysterography find their place in a complete search for structural anomalies and are of much value in determining the status of genital development.

TREATMENT

The treatment of primary amenorrhea necessarily entails an attack upon the underlying cause. Therapeutic measures, whatever they may be, should have a rational basis and should entail no danger to gonadal function. Prophylaxis is of the utmost importance. The parent and the family physician should be on the lookout for developmental faults and depressive states in young girls approaching the age of puberty. If the basic trouble is corrected before irremediable changes have occurred a permanent amenorrhea may sometimes be averted.

Medical and Hygienic. General medical measures directed toward the elimination of all subnormal manifestations, whether intimately or remotely connected with gonadal function, are indicated before any other plan of treatment. These may be effective in establishing normal menstrual function, particularly in cases in which some degree of sexual maturity has been attained.

This approach is specifically indicated in the amenorrhea due to debilitating diseases, or to any other fault of endogenous or exogenous origin which depresses the organism. Foci of infection, systemic disease, metabolic disturbances and other adverse influences should be eradicated.

Dietetic. The correction of nutritional faults is of prime importance.

The average normal individual selects his food according to his taste and this provides an adequate variety and amount of nourishment. In the amenorrheic girl there may be a faulty selection, ingestion or assimilation of food, either from conditions of physical and mental health or from economic situations or environment. Even when the individual is of normal weight and the food intake presumably adequate, the very fact that the menstrual function is lacking makes it possible that certain food essentials may be deficient.

In addition to the usual fruits, cereals, vegetables, meats and sweets of the table, the patient should add a selection of foods

especially rich in vitamins A, B and E, the ones which seem to be especially needed for the reproductive functions. The necessary vitamins may be given also in other forms as supplied by the trade.

In the *underweight* a high caloric diet rich in vitamins may be prescribed with due regard for the digestive and assimilative powers of the individual. The relative proportion of food elements including vitamins must of course be preserved. Sometimes the appetite and the assimilation of food are benefited by a daily injection of insulin, 5 units, just before the principal meal of the day, which should be rich in carbohydrates. Some restriction in physical and mental activities, definite periods of rest, fresh air and sunlight, natural or artificial, are conducive to successful results.

When anemia is an associated finding, iron, arsenic and liver extract, given with vitamin B complex, may be of much benefit.

By thus increasing the nutritional store of the body we may ensure an adequate supply of the basic substances from which the anterior pituitary and ovarian sex hormones are manufactured.

If these measures are all observed thoroughly, if a health promoting regime is prescribed, if the patient is lifted to the peak of physical condition and placed under the most favorable conditions of living, menstruation and some of the other evidences of puberty may make their appearance. Under such circumstances, of course, we may ask whether the essential endocrine background was not always there but required time and an improvement in general health for its development.

When the amenorrhea is associated with *obesity* an appreciable reduction in weight may be of value in establishing menstrual function; exactly how this is accomplished is obscure.

To effect a gradual loss of weight, a diet low in calories but one which insures an adequate supply of the basic food elements as well as essential minerals and vitamins, should be instituted. The coöperation of the patient, her acquaintance with caloric values and an estimation of her weight every day will be conducive to success.

Besides limiting the caloric intake, some attention should be paid to water retention. The tissues of the obese often contain an excess of fluid. We may help by restricting the water intake and by promoting water elimination. The prescription of epsom salts or other saline cathartics twice a week and the administration of sodium citrate or other alkaline diuretic in concentrated form may be of value.

Massage, exercise and sweat baths will promote elimination by the skin.

Endocrinologic. We are quite immediately concerned with the therapeutic possibilities of improvement when the endocrine background is faulty. We must find a way of stimulating the production of sex hormones in the anterior pituitary.

There seems to be little doubt that the correction of functional disturbances of the thyroid may have a favorable influence upon gonadal and menstrual function. The empiric use of thyroid substance is considered by many observers one of the most effective methods available for the treatment of functional amenorrhea. The best results have been obtained in amenorrhea associated with obesity or with a depressed metabolic rate. Thyroid substance should be given a trial even when the basal metabolic rate is normal, for mild hypothyroidism may depress gonadal function without any other clinical evidence of thyroid deficiency. The manner in which the thyroid hormone aids in establishing menstrual function is not clear. Some believe that it acts by increasing the metabolic activity of the organism as a whole, and with it that of the ovary and its endocrine regulators.

The thyrotropic principle of the anterior pituitary gland deserves mention in the treatment of amenorrhea associated with thyroid hypofunction. At present there is not sufficient evidence to permit an estimate of the value of this substance in the human, and further clinical tests are neces-

sary. The possibility that protracted administration may create a refractory state due to the formation of antihormones which nullify its effect, must be kept in mind.

Sex Hormones. For the human being a really potent preparation of the sex hormones of the pituitary has not been found. The anterior pituitary-like gonadotropic hormones derived from the placenta or from pregnancy urine or blood may be administered as substitution products for the purpose of stimulating the endocrine and the ovogenic activity of the ovaries. Controlled studies with anterior pituitary gland extracts seem to show that little can be accomplished in the human with the preparations now available.

The spectacular effects produced with these preparations upon the gonads of lower animals have encouraged their extensive use for the treatment of amenorrhea associated with sexual immaturity or other manifestations of pituitary deficiency. While numerous reports lauding the efficacy of gonadotropic hormones have appeared in the literature, the few systematic attempts to ascertain their effect upon the human ovary leave us in doubt as to a stimulative effect.

Pregnant Mare's Serum. The most promising preparation thus far offered for clinical use is that derived from the serum of pregnant mares. Much attention is being given to this substance at the present time. Several observers have noted evidence of follicular growth and ovulation following its administration in the normally menstruating human and subhuman primate. Evidence that it is equally effective in patients with hypogonadism is limited and not completely convincing.

Hamblen has recently reported the case of a 17 year old girl with primary amenorrhea in whom mare's serum hormone therapy was employed after anterior pituitary gland extract had failed to elicit a response. A total of 1000 mouse units was given over a period of twenty days; this was followed after a lapse of one month by a total of 3,400 mouse units over a period of six weeks. During the course of treatment, enlargement of the ovaries and growth of the uterus was noted. At the end of treatment, endometrial biopsy revealed a pregravid type of endometrium and was followed two days later by bleeding. No further treatment was given but periodic bleeding occurred thereafter and rapid development of secondary sex characters took place.

A single case, though significant, justifies no definite conclusions as to the value of mare's serum therapy in primary amenorrhea. It must be noted that in Hamblen's patient a certain degree of sexual development had already taken place, as evidenced by the presence of axillary and pubic hair, and by the fact that the internal and external genitalia were of the juvenile rather than of the infantile type. In view of the fact that the patient was 17 years of age and therefore not yet beyond the limits of late puberty (known to occur as late as the twenty-first year), the possibility of spontaneous establishment of menstrual function must be taken into consideration.

Though Hamblen's experience does not by any means conclusively establish the efficacy of mare's serum hormone in primary amenorrhea, it certainly suggests that this substance is worth a trial.

It must not be forgotten that even a potent gonad-stimulating preparation will be of no value if the amenorrhea is due to some inherent defect which renders the gonads refractory to stimulation.

Estrin and Progestin. The products of the Graafian follicle and of the corpus luteum may be used as substitution therapy in an attempt to effect the normal influence of these substances on the genital tract and the secondary sex characters.

The use of estrin or of estrin followed by progestin in the treatment of amenorrhea is based upon the experimental and clinical observation that an adequate dose of these hormones will induce endometrial alterations similar to those seen during the follicular and the luteal phases of the

normal menstrual cycle. Upon completing a series of injections of estrin (total dose 1,000,000 international units over a twenty-one day period) followed by progestin (total dose of 35 or more rabbit units over a seven day period), there follows within a short time disintegration and bleeding from a pregravid type of mucosa.

Unfortunately the bleeding so induced has not been associated with any real improvement in gonadal function. It is probable that ovarian hormones have no direct stimulative effect upon the ovary. Some observers are hopeful that large doses of estrin may stimulate the gonads indirectly by way of the anterior pituitary and base their belief upon recent reports that rodents respond to intensive treatment with estrogenic hormones (for example 200 r.u. daily for twelve days) with ovulation and corpus luteum formation. Convincing evidence of a similar action in the human has not been found.

Some observers recommend the use of the estrogens (50,000 international units twice weekly) to develop and vascularize a hypoplastic uterus. Though undoubtedly effective for this purpose, little may be gained with such therapy in primary amenorrhea for the reason that if the uterus is hypoplastic the ovaries may be hypoplastic also. Unless their condition can be improved simultaneously, the induction of uterine growth is of no avail.

Not only are the estrogens of little value in such cases but they may actually do harm, for the huge doses required to stimulate uterine growth may further depress the already deficient ovary. We reluctantly conclude therefore that the ovarian hormones (estrin, progestin) although effective in stimulating endometrial growth and menstrual bleeding, are of no permanent benefit to the anterior pituitary or the ovaries. There is not much use in administering them just for the sake of producing uterine bleeding if a repetition of treatment is necessary for a second bleeding. Forcing one period or several periods by estrin and progestin does not seem to motivate either the ovaries or the pituitary. The repeated use of substitution hormones in large dose may discourage and reduce the natural production. For the present therefore we do not employ them.

Roentgen Radiation. The Roentgen ray has been proposed for the purpose of directly stimulating the pituitary and the ovary. Although successful results have been reported by others from *x*-ray "stimulation" of the anterior pituitary we cannot be sure that we have seen any effect. It is admitted as a general proposition that the *x*-ray is depressing and not stimulating. A suggestion has been made that radiation increases the action of the anterior pituitary in the production of sex hormones by depressing certain factors inhibiting to the production of those hormones. We are skeptical about influencing the anterior pituitary favorably unless there is a demonstrable lesion of the pituitary or the midbrain regions.

We never use even the smallest dose of *x*-ray on the ovaries. Sometimes prompt and excellent results follow its use, but sometimes it has a disastrous effect. It is particularly hazardous in primary amenorrhea where the ovary is already deficient and even a very small dose may destroy the last vestige of function.

Curettage. Curettage as a surgical therapeutic procedure has often been abused. It is not advised in the young woman until the other measures of which we have spoken have been tried unsuccessfully. At a suitable time, however, it may be a wise procedure and it often serves a number of useful purposes. First of all, the opportunity of measuring the length of the uterine cavity and of determining the exact state of development of the uterus and adnexa may be possible only after anesthetizing the young patient. Such information is of course valuable if for no other reason than as a matter of prognosis. Secondly, an examination of the uterine scrapings gives a most reliable index of ovarian function. Thirdly, the mechanical irritation produced by dilatation of the

cervix and scraping the walls of the endometrial cavity may benefit the reproductive functions. This is in line with the observation that coitus as well as mechanical irritation of the cervix in the rabbit induces ovulation, and that there is improvement often in the menstrual function after marriage which apparently is due to the stimulating effect of sexual intercourse.

CONCLUSIONS

In patients with fair development of the secondary sex characters and without endocrinopathic stigmata, primary amenorrhea often yields to treatment.

The utmost and the closest attention should be paid to the general health as well as to the weight, the diet and the habits.

The interest and coöperation of the patient herself should be aroused. The nearer she can be placed to normalcy in every physical and mental respect the greater will become the capacity of her own endocrine glands to manufacture the hormones that she needs. Patience, persistence and the course of time will bring the desired results.

In patients with poorly developed sex characters or with endocrinopathic stigmata, primary amenorrhea may be incurable.

Thyroid substance, especially in the obese and in the hypothyroid, is often of value; the thyrotropic hormone may be given a trial.

Estrin and progestin are not likely to be of permanent help and may do some harm.

The possibility of stimulating the anterior pituitary with the *x*-ray seems very remote; the success apparently attending its use by some observers may be explained on other grounds.

Roentgen ray treatment of the ovaries is some times followed by menstruation but it is a dangerous procedure; one never knows when it may destroy what little ovarian function there is and turn the scales against the patient.

Pregnant mare's serum may be tried on logical grounds since its effect more closely approaches that of the gonadotropic principles of the anterior pituitary than any other substance we possess.

Curettage affords us the most reliable index of ovarian function and may promote the development of that function by mechanical irritation. It should not be used until simpler means have failed and it becomes apparent that every therapeutic resource must be utilized.

TREATMENT OF TRICHOMONAS VAGINALIS*

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LEUCORRHEA is one of the commonest complaints among gynecological and obstetrical patients. From the symptomatic standpoint, it is usually the first to arise and the last to disappear. Davis,[1] in examining 1000 female patients, found that 33 per cent had some type of discharge. This is about the percentage in my practice and in the gynecological clinic of the Jefferson Davis Hospital, Houston, Texas. Trichomonas vaginalis is one of the most common causes of leucorrhea, but had been overlooked until our research at the University of Texas School of Medicine.

The first case of trichomonas vaginalis reported in the United States was by George Dock[2] in Galveston, Texas, where most of this research was carried out. The first papers on trichomonas vaginalis were reported by Donne[3] in 1837 and later ones by Kunstler[4] in 1893 and 1894, by Benson in 1912, DeLee[5] in 1920, Reuling[6] in 1921, Hegner[7] in 1925, Bland and Rakoff[8] in 1932. Since that time many American authors, such as Hesseltine,[9] Drabkin,[10] Buxton and Shelanski,[11] and the author[12] have added to the literature.

Incidence of Trichomonas Vaginalis. In 1932 at the John Sealy Hospital, Galveston, 500 consecutive women coming to the outpatient clinics of the hospital were examined. There were 187 positive cases of trichomonas vaginalis, a percentage of 37.4. There were 300 negro and 200 white females; 46.3 per cent of the negro females, and 24.0 per cent of the white females harbored the organism. These patients ranged from 11 to 52 years of age. The largest percentage of positive cases of trichomonas vaginalis lay between the ages of 19 and 33 years with the largest single group at 23.

According to the author's statistics, based upon the examination of over 10,000 women, trichomoniasis was present in 37.5 per cent of the gynecological and obstetrical patients in Galveston, Texas, a seaport, and in only 27 per cent of the same class of patients in Houston, Texas, 52 miles inland. The author has examined more than 25,000 female patients for trichomonas vaginalis during the past eight years and the percentage of patients found positive was 25.5 per cent.

Urinary Infections. Flashkamp[14] found trichomonas vaginalis in the urine in one out of 250 patients examined, and Sayer[15] in 27 per cent of 212 patients examined. Sayer believes the bladder to be the normal habitat for trichomonas vaginalis. In our resistant and obstinate cases, we find trichomonas vaginalis more often in the bladder. Whenever one fails to cure trichomonas vaginalis by the routine method, such as floraquin and vinegar douches, then at the same time as the vagina is treated, the bladder is irrigated with boric acid followed by the instillation of argyrol.

Signs and Symptoms. The patient usually complains of a discharge or "whites" with an itching and burning, or chafing, of the external genitalia and inner aspect of the thighs. No other discharge produced by the vaginal mucosa and no other microorganisms besides the trichomonas vaginalis causes a scalding sensation of the vagina, vulva and perineum.

The discharge is usually thin and creamy in color, but it may be thick and yellowish. At times it is difficult to distinguish trichomonas infection from gonorrheal infection. The discharge of trichomonas vaginalis usually resists all types of treatment, but it may sometimes be checked by

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simple douching, or with one of the common antiseptics on the market advocated for this protozoan infection. However, the discharge soon recurs as profusely as before. There is an increase in the discharge and burning at the beginning and more so at the end of menstruation, with less burning and itching during the period.

Some patients have as their chief complaint burning on urination, others dispareunia, still others difficulty in walking due to the marked scalding of the exposed surfaces of the thighs. The most common complaint is a discharge that causes an itching of the external genitalia. In our study of more than 5000 cases of pruritus vulvae in the gynecologic clinic, 90 per cent were due to trichomonas vaginalis, ½ per cent to monilia albicans of the vagina, and the rest to various rare causes.

On examination of the vulva one sees an excess of discharge if the patient has not taken a douche within the past hour. In some cases there is very little discharge. In most cases the discharge will run out of the vagina on separation of the labia. In some cases many scratch marks give evidence that the patient has had a great deal of itching. There may or may not be an associated cervical discharge.

In the acute cases of trichomonas vaginalis, there is a diffuse reddening of the vulva, vagina, or cervix, similar to that noted in any other acute vaginitis.

In the chronic cases of trichomonas vaginalis there may be the so-called "colpitis granulosa," "strawberry vagina" or "salt and pepper vagina." This is characteristic of trichomonas vaginalis, we believe. In eight years of leucorrhea research, we have not seen it in any other vaginal conditions.

Diagnosis. The patient is instructed not to take a douche for twenty-four to forty-eight hours before coming to the office for an examination for the cause of her leucorrhea. If it is her first visit, a smear is made, even if she has taken a douche and a microscopic examination for organisms made. She is instructed to return the next day without douching for a second vaginal smear study.

Two cotton applicators are inserted into the posterior fornix of the vagina before any vaginal or speculum examination is made. The two applicators are placed in 0.5 c.c. of ordinary tap water in a test tube, and are turned around several times in the tube in order that the secretion may be loosened somewhat. A thick smear is then spread across the entire length of a clean slide. Movement is looked for under low power. If the patient has not taken a douche and if lubricating jellies have been omitted, one will observe in a positive case of trichomonas vaginalis many organisms moving around. For more detail the higher power of the microscope may be used.

Physiology of the Vagina. The physiology of the normal vagina should be considered before the logical approach to treatment may be arrived at. We have outlined treatment in this paper after an exhaustive study of vaginal pH, epithelial cell height, vaginal bacterial flora, glycogen contents of the epithelial cells, and the way glycogen is broken down into acids in the vagina.

The vagina is a tubal organ which varies in length and size. It is an organ where sperm are deposited, a birth canal, and conveys menses from the cervix to the introitus.

At the introitus, there is a normal drying mechanism of the secretion that passes by osmosis through the mucosa of the vagina and of the secretion that comes from the cervix. Most of the vaginal secretion is produced in the vagina, but a small amount of it comes from the cervix. If the secretion is in excess of that which can be normally dried at the vulva, the patient usually complains of a discharge.

The reaction of the normal vagina is acid, as tested with nitrazine paper (Squibb), Hellige, Wulff or the electrometric method. The pH varies from 3.9 to 4.4. We have tested pH in over 5000 vaginas in our clinic; for all practical purposes the normal pH may be considered about 4.0.

In view of these observations, all medication should be of pH approximately 4.0 or below. Precautions should be taken not to produce a pH so low that the vaginal mucosa will be burned. I have found that a pH of 2.9 is most suited for douches, and that sugars, such as glucose, maltose, saccharose, lactose, or a combination of the four, are of great benefit in the treatment of most vaginal infections.

A stained biopsy of the normal vaginal mucosa shows about forty-five to fifty-five cell layers in height. Sections of normal vaginal mucosa stained with Best's carmine stain or other glycogen staining methods, show an abundance of glycogen granules in the epithelial layers. The upper layers of the vaginal epithelial cells are well vacuolated and these vacuolated areas are receptacles for glycogen which is picked up from the blood by the vaginal epithelial cells. The glycogen is broken down into glucose and finally into lactic acid, which is the normal acid of the vagina. This is carried out by enzyme action and the action of Döderlein bacilli. Other organic acids are also produced.

The application of Lugol's solution to the normal vaginal mucosa produces a deep mahogany color, due to the action of iodine on glycogen. If there is a loss of glycogen, no change in color results; if there is a decrease in glycogen, there is decrease in the intensity of the mahogany color.

In infections of the vaginal mucosa there is a depletion or almost complete loss of glycogen, with less mahogany color formation and less acid reaction. In an infected vagina there is a positive decrease in the amount of glycogen stored in the epithelial cells.

A fresh or stained smear from a normal vagina shows many fat, stick-like organisms (Döderlein bacilli) and many large clumped epithelial cells with small nuclei. The epithelial cells stain normally. There are few pus cells or none at all.

If a smear from an infected vagina is made, whether the infection is due to trichomonas vaginalis or some other organism, few, if any, of these Döderlein bacilli are seen. We will also see many shapes, forms, and kinds of micro-organisms, such as streptococcus, staphylococcus, and colon bacillus. The epithelial cells do not take the stain so readily and the epithelial cells are no longer in clumps, but are broken up into fragments. It may be said, then, that in an infected vagina there is a mixed vaginal flora, with a positive decrease in the Döderlein flora normally present.

There is, therefore, a state of deficiency of four physiologic elements: (1) hypo-acidity; (2) hypo-glycogen; (3) hypo-epithelium; and (4) hypo-Döderlein.

Acidity and Alkalinity and Growth of Vaginal Micro-Organisms. To substantiate the above research, eight cases of acute vaginitis with a very foul malodorous discharge were surveyed in an experiment. The patients were told not to take douches, to omit coitus, and not have any vaginal treatment for two weeks. External plain water washes were allowed. By sterile technique, all the vaginal secretion that could be collected from the vagina was placed in 0.5 c.c. of warm sterile water in a sterile test tube. From this solution a smear was made on agar of a pH of 2.8, 3.6, 4.4, 5.4, 5.5, 6.0, 7.0, 7.2, 7.6, and 8.0.

Table 1

Case	pH of Vaginal Secretion	pH of Media and Growth of Vaginal Micro-Organisms										Broth and Agar Control
		8.0	7.6	7.2	7.0	6.0	5.5	5.4	4.4	3.6	2.8	
1	6.8	8x	8x	6x	5x	3x	3x	2x	0	0	0	7x
2	6.0	8x	8x	5x	3x	3x	0	0	0	0	0	8x
3	6.8	8x	7x	5x	4x	3x	0	0	0	0	0	8x
4	6.5	8x	8x	6x	4x	3x	3x	0	0	0	0	8x
5	5.9	8x	8x	6x	4x	3x	3x	0	0	0	0	8x
6	6.9	8x	8x	8x	4x	3x	3x	2x	0	0	0	8x
7	6.6	8x	8x	5x	4x	3x	3x	2x	0	0	0	8x
8	6.3	8x	8x	5x	4x	3x	3x	2x	0	0	0	8x

0 = no growth.
8x = profuse growth.
2x = slight growth.

Bacterial growths were most abundant at a pH of 7.6 and 8.0 and as the pH became more acid, the bacterial growth became less and less. There was no growth at a pH of 5.5 in two cases, 5.2 in four cases, and 4.4 in

all cases. Controls were used and growths were most abundant at pH of 7.6 and 8.0. There were no growths at a pH of 4.4 or below. Staphylococcus and colon bacillus did not grow at a pH of 5.0 or below. (Table I.)

were instructed to insert one dose of this jelly into the vagina at night and in the morning. Vaginal cultures were made after jelly of different pH was used in the vagina from three days to six months. The results were similar to those obtained when the

TABLE II

Drug	Amount of Drug	Amount of Water	Microscopic Results	Clinical Results	pH
Sodium perborate	3 heaping teaspoonfuls	Quart tap water	No death	Poor	10.0
Borax	3 heaping teaspoonfuls	Quart tap water	No death	Not good	9.0
Sodium bicarbonate	3 heaping teaspoonfuls	Quart tap water	No death	Not good	8.0
Dilute sodium hydroxide	.....	In tap water	No death	Not good	8.0
Magnesium sulfate	3 heaping teaspoonfuls	Quart tap water	No death	Not good	7.5
Sodium chloride	1 cup	Quart tap water	Stops mobility immediately. No death.	Fair, does not destroy trichomonads	7.4
Silver picrate	4 gr.	5 c.c. tap water	No death	No death with 4 or less gr.; 5 gr. death. Fair.	7.3
Potassium permanganate	3 tablets	Quart tap water	Death	Fair	7.3
Boric acid	3 heaping teaspoonfuls	Quart tap water	No death	Not good	6.1
Caprokol	1 drop	In vaginal smear on slide	No death	Not good	5.9
Anayodin	8 c.c.	In tap water	No death	Not good	5.8
Verazeptol	1 teaspoonful	Quart tap water	No death	Not good	5.8
Lugol's solution	2 heaping teaspoonfuls	Quart tap water	Death	Good	5.6
Dilute HCl	.....	In tap water	Death	Good	5.0
Orthogynol	1 drop	In vaginal smear on slide	Death	Good. Death immediately	4.5
Acetarsone	1 gr.	5 c.c. tap water	Death	Good	3.9
Alum	1 gr.	5 c.c. tap water	Death	Good, but dries vagina too much	3.6
Vinegar	5 tablespoonfuls	Quart tap water	Death	Good	3.5
G. C. douche powder	3 heaping teaspoonfuls	Quart tap water	Death	Good	3.0
Floraquin	¼ tab.	5 c.c. tap water	Death	Death immediately. Good	2.9
Acetylsalicylic acid	5 gr.	5 c.c. tap water	Death	Good	2.9

Note: Nitrazine paper (Squibb) is ideal to determine the pH of vaginal secretion and douches.

Jelly at Varying pH. Sixteen other patients with acute vaginitis and foul malodorous discharge were given jelly at a pH of 2.0, 2.5, 3.5, 3.7, 4.0, 4.5, 4.6, 4.7, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, and 9.0. The patients were instructed not to take douches, to omit coitus, and to have no type of treatment in the vagina. They vaginal micro-organisms were cultured on media at different pH, as given above.

Regular ortho-gynol jelly was used in sixty patients with nonspecific infections and found to be efficient clinically, as well as when tested culturally and under the microscope in the laboratory. The jelly is soft and easily applied and was found

to be satisfactory for the treatment of nonspecific vaginal infections in 89 per cent of the cases.

The first work along this line was done by Döderlein in Germany. Then came the work of Cruickshank and Sharman of England, followed by our work in Houston and Galveston. Since my results have been published, other investigators have made similar reports.

Acidity is the most important factor in the treatment of trichomonas vaginalis and in any vaginal infection. Those who are at present using antiseptics without regard to the pH of the drug would find their results greatly improved if an acidifying agent were used.

I have used almost every drug advocated for the treatment of trichomonas vaginalis, and found that they all give approximately the same results unless they have a low pH. Most drugs advocated for trichomonas vaginalis gave us a 70 to 80 per cent clinical cure in from three to six months.

Most of these drugs, however, have never been tested directly in contact with the trichomonas under the microscope. We have attempted to correlate the microscopic and clinical results, after testing the pH of the solutions to determine whether there was any relationship between the clinical results and the findings under the microscope, and between the pH and the death of the trichomonas vaginalis.

The following drugs were tested: silver picrate, floraquin, borax, vinegar, sodium chloride, sodium bicarbonate, sodium perborate, potassium permanganate (10 gr.), boric acid, and a gonorrheal douche powder containing alum, zinc sulfate, menthol, and boric acid. Magnesium sulfate, alum, acetarsone, acetylsalicylic acid, ortho-gynol jelly, dilute hydrochloric acid, verazeptol, caprokol, anayodin, dilute sodium hydroxide, and Lugol's solution were also tested. (See Table 1.)

Death of trichomonas vaginalis usually occurs when the pH is 5.6 or lower. As the alkaline side is approached, the drug has less effect. At pH 8.0 and 9.0 the trichomonads were motile and cell division took place. They lived longer and were more motile in an alkaline medium. Thus trichomonas vaginalis can live easily in the cervical canal, which has a pH of 7.2 to 9.0. I am of the opinion that the organisms pass into the cervix and live. This is one of the reasons for recurrences, as, after treatment is discontinued, they emerge from the cervix and reinfect the vagina. They also occur in greater numbers and more frequently in urine which is alkaline or near the alkaline side. Trichomonas vaginalis can live and multiply in most normal or abnormal urine of the bladder. In many resistant cases I have found the recurrence to be due to reinfection from the bladder.

In the male urethra, under the prepuce, and in the prostate, the secretion has an alkaline pH of 7.2 to 7.5. It is possible for the trichomonas to live there and reinfect the partner at coitus. I have reported thirty-eight such cases.

Treatment. After a positive microscopic diagnosis of trichomonas has been made, or whenever a patient complains of a foul malodorous discharge that causes an itching or burning of the external genitalia, and in all vaginal infections, the following treatment is advocated: the vulva, vagina and perineum are gently washed with vinegar water (five tablespoonfuls in two quarts of water) and dried. One to 2 drams of floraquin powder are then blown into the vagina or four to eight floraquin tablets are inserted, encircling the cervix, with a small plug of cotton inserted at the introitus. The patient is given a prescription for twenty-four floraquin tablets, one to be inserted each morning and one each night. Instructions should be given not to douche during this period. Perineal pad and external washes are to be used as necessary. After twelve days, vinegar water douches (5 tablespoonfuls of vinegar to 2 quarts of water) are to be taken twice a day between and during the next three menstrual periods and up to the fourth menstrual period. Acetic or lactic acid (5 per cent) may be used. At the end of the fourth

menstrual period a fresh vaginal smear is made for trichomonas vaginalis, and if found negative the patient is pronounced cured. If the smear is positive, the treatment is resumed.

Following each menstrual period for two to five days, one floraquin tablet is inserted morning and night with vinegar douches as needed for cleanliness.

The patient is instructed to insert two floraquin tablets as soon as the slightest itching or discharge returns and to insert one tablet night and morning for six days.

The patient returns twice each week for two weeks for observation as to how the infection is progressing. Floraquin powder insufflations are used as needed.

In acute cases of trichomonas vaginalis, pruritus vulvae, or vaginitis with a great deal of tenderness, 1 to 2 drams of floraquin powder are blown into the vagina every day until the soreness is gone. Due to the soreness of the vaginal tract an acid jelly (ortho-gynol) can be inserted night and morning as a home treatment. After the acute stage has subsided, one floraquin tablet is inserted night and morning as the home treatment.

In 400 cases of trichomonas vaginalis in private practice and over 4,000 charity cases at the Jefferson Davis Hospital, 94 per cent were cured by this method. Antiseptics and the various unscientific procedures are no longer used or advocated. We now have a sound scientific method which gives us excellent results.

Shelanski and Buxton advocate silver picrate, but it has an alkaline pH. I have seen 400 private patients for the treatment of trichomonas vaginalis and 98 per cent of them had had from one to several courses of treatment with silver picrate, and all were still positive for trichomonas vaginalis. Silver picrate causes in many cases a peeling of the vaginal mucosa of the wife and of the penis of the husband. We do not advocate any alkaline preparations. Kaldor[13] suggested concentrated salt douches. This has been found to be no more efficient than the ordinary drugs or antiseptics already advocated.

We have used the lactose citric tablet but found that too many patients could not stand the smarting and burning from the citric acid. Tartaric acid does not produce the smarting and burning and is advocated instead of citric acid. This preparation has a pH of approximately 3.5. If one ascertains that the pH of the powder, solution, jelly or tablet to be used is lower than 5.6, a higher percentage of cures will result.

Hibbert's streptococcus subacidus vaccine has been used in fifty patients, two of whom obtained relief from their itching. The itching returned, however, in two to three months.

CONCLUSIONS

1. Solutions, tablets, powders or jellies of pH 5.0 or lower should be used. Drugs with pH above 5.0 should not be used.

2. Vinegar (5 per cent acetic acid), acetarsone, Lugol's solution, glucose-lactose pH 2.9 tablets and powder (floraquin), alum, ortho-gynol jelly, lactic acid, or any similar solution of pH 5.0 or less is worth using.

3. The above drugs were destructive to all the abnormal microorganisms of the vagina and did no harm to the normal vaginal organisms.

4. Clinical results corresponded directly to the pH in the clinical cases of more than 4,000 women treated with the drugs listed above during the last seven years.

5. Silver picrate pH 7.3 is not advocated. Ordinary dry sieved cornstarch or kaolin in powder form, accompanied by vinegar douches as the home treatment, will give better results. These are more reasonable in cost also.

6. In a high percentage of cases it is the acidity of the drug that destroys vaginal micro-organisms rather than its specific bactericidal action.

7. One or 2 drams of floraquin powder are blown into the vagina or four to six tablets of floraquin are inserted at the first visit. The patient is instructed to insert one

tablet night and morning with no douches for twelve days. Only external washes are allowed for cleanliness. Vinegar douches, are taken three times a day during the menses.

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THE MENOPAUSE

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THERE are various types of true climacterics: the natural, the radiologic, and the surgical. The natural menopause may be subdivided into the precocious and the usual; the latter occurring at or about the age of 47. The radiologic menopause can be brought about by intrauterine radium or the use of the Roentgen ray, both of which destroy the function of the ovaries. The surgical menopause is the quickest and of course is the most complete. In the natural or radiologic menopause ovarian tissue is still present and it is possible to imagine a follicle seemingly inactive being reactivated. Complete death of all follicles may not occur and at a later period menstruation may start over again.

DIFFERENTIAL DIAGNOSIS

The menopause, true ovarian failure, can easily be confused with another type of cessation of the catamenia, that is, the amenorrhea due to pituitary failure. In this type of amenorrhea absence of hot flashes is a characteristic clinical symptom. The possibility of pituitary failure must be considered in all cases of amenorrhea. It can be differentiated in the laboratory from ovarian failure by the absence of the follicle stimulating hormone in the urine. A low 17 ketosterone determination* in the urine in addition to absent follicle stimulating hormone is practically confirmative of pituitary failure. Debilitating disease is frequently accompanied by ovarian hormone suppression, but this is not the true menopause. Toxic thyroid disease and myxedema are often associated with amenorrhea. Lack of ovarian development is accompanied by lack of menstrual function; however, this should not be interpreted as the menopause but rather as a primary ovarian amenorrhea. The menopause means cessation of menstruation following failure of a once active ovarian function.

* The 17 ketosterone determination is a colorimetric procedure used as a measure of secretion of the androgen-like substance of the adrenal cortex. Therefore lack of it is interpreted as indicating anterior pituitary failure, at least of the hormone that stimulates the adrenal cortex.

SYMPTOMS

The symptoms of all menopauses are similar. Usually there is an occurrence of hot flashes, though many patients never seem to have had them. Dizziness is frequent, as are night sweats and depressions. Hot flashes may commence in any region of the body from extremities to face but usually end up by causing a marked facial vasomotor disturbance. Patients have a sensation of suffocation and oppression, often rush to a window, or begin to fan themselves. It is extraordinary how infrequently hot flashes are noticed in friends, yet each patient is violently conscious of her own flashes and is embarrassed by them. This phenomenon may be very infrequent, frequent, or very frequent—ranging from one to thirty each twenty-four hours. Night sweats are common and cause concern because of the possibility of contracting cold or pneumonia. It is necessary for certain patients to get up out of bed and change their night clothes because of the excessive perspiration that has occurred with the flashes.

Dizziness is a very common symptom and is often diagnostic of ovarian failure. This symptom is very distressing because it causes a certain amount of insecurity. Some women feel unsafe driving a car or

crossing the street. Depression is usual and may range from a feeling of blueness to a deep and melancholy depression.

Personality changes occur; the simple sweet woman may become aggressive and domineering and the masculine woman may become sensitive and kindly. Some women lose all libido, and yet others have an enormous increase in sex desire. Occasionally with loss of normal sex feeling abnormal desires commence.

Physical characteristics may change in some instances; occasionally a woman becomes gross and obese. Increase of weight is often due to laziness and overindulgence following surgery or radium. The patient never recovers her pride and uses her operation and artificial menopause as an excuse to avoid excessive activity. And she overeats. Abnormal growth of hair is not common, but with lack of estrin and a comparative increase in androgen this may be expected.

All sorts of changes may occur but we all know that most climacterics are not violent, depressive, masculine, or productive of grossness, especially when the great number of gentle, sweet, old ladies is considered. Increased ability, energy, and a delight at relief from "the curse," should assure most women that the menopause holds no terrors. A perfectly natural state, a release from fluctuating glandular waves, the menopause should be and in most instances is the most comfortable time of a woman's life.

PATHOLOGY

In the menopause certain fundamental changes occur. The primordial follicles and ova vanish because they are all used up or disappear because of some unknown reason. Graafian follicles fail to develop and the ovary becomes fibrous. The stroma changes from a vascular, active connective tissue to a tough fibrous or even hyaline type. The ovary finally is a small wrinkled organ without signs of activity.

Following cessation of ovarian function the breasts atrophy as there is no longer any active ovarian stimulation. The breasts take on a characteristic lumpy, doughy feel characteristic of the menopause. The uterus atrophies and is inactive. It resembles the juvenile uterus, with the cervix the same length as the fundus. There is an increase of connective tissue and decrease of smooth muscle. The endometrium shrinks and the glands that are left lie parallel to the uterine muscle rather than perpendicular to it. Frequently but one layer of cells lines the endometrial canal. The cervix becomes smaller and often more pointed. At this time a scarred cervix may become very narrow and any secretions from the endometrium may lack drainage and pyometrium may develop. The vagina atrophies and large round cells or typical menopause cells are found on vaginal smears. The lack of succulence and vascularity of the mucous membrane of the vagina is conducive to infection and vaginitis often occurs, followed by adhesions, a cause of partial obliteration of the vagina. The vulva also changes, the skin becomes dry and thin. Sometimes the clitoris is involved in cicatrices followed by infections in the region of the prepuce. Vulval atrophy may be severe, and subsequent infection may be responsible for leucoplakic vulvitis, the end result of which may be typical kraurosis. The urethra is involved in the vaginal atrophy and may become tube-like and narrow. Incontinence and frequency of urination may follow. The skin about the anus may become tough and fibrous and cracks and fissures and small hemorrhoids may result.

The pituitary gland hypertrophies and secretes an excess of follicle-stimulating hormone. Other glands may have an increase of secretion but this increase may be only relative. It is well known that thyrotoxicosis and myxedema often occur at the time of the menopause. Hypertension is common at this time and a cause for it may be found in the adrenal medulla, which may oversecrete and cause vasomotor changes. If masculinization occurs it may be due to a relative increase of

androgen or to an actual increase in secretion of the adrenal cortical hormone.

The menopause caused by cessation of ovarian function is usually compensated for by the end of the first year. The greatest number of women go serenely on, but others have severe and devastating difficulties and some are changed permanently.

BIOLOGIC CONSIDERATIONS

In studying the menopause biologically two findings are definite. There is nearly a complete absence of estrin; and an increase in the follicle-stimulating hormone (usually called F.S.H.) of the anterior pituitary gland. In many patients with menopause symptoms some small amount of estrin can be demonstrated. The source from which it comes is not quite clear, but it is possible that the adrenal cortex may be responsible, or there may be some metabolic breakdown of androgen or a change in cholesterol metabolism. This amount of estrin is very small and it does not affect the menopause symptoms to any great extent. It is conceivable, however, that certain women who have few symptoms may be among those who have large amounts of extra-ovarian estrin. F.S.H. is definitely increased and certain investigators believe that the seriousness of menopause symptoms is in proportion to the amount of this hormone. It is true that the presence of estrin in the urine of menopause patients does not necessarily mean a lessening of symptoms, but lowered amounts of F.S.H. are of great importance. Pituitary failure may be considered a cause of amenorrhea or suspected menopause when there is no F.S.H. in the urine, for in ovarian failure it should be present. If the determination of the 17 ketosterone, which is indicative of androgen in the urine is low, it can be considered as indicating lowered adrenal function. This probably is indicative of lowered pituitary function and if, in addition, in cases of amenorrhea there is no F.S.H. in the urine, pituitary failure is probably present.

The presence or absence of F.S.H. differentiates most cases of amenorrhea, but determinations of 17 ketosterone and of estrin help point out the responsible gland.

TYPE OF MENOPAUSE

The natural menopause may be divided into two types, the precocious and the normal. The menopause in young women is considered precocious. In this type the ovary fails or atrophies and typical menopause symptoms commence—hot flashes, etc. F.S.H. will be positive, estrin practically absent. This type should respond to treatment and the hot flashes cease. In such cases the ovaries are usually very small and atrophied and there is a lack of primordial follicles. The treatment of this type of menopause is that of ovarian hormone substitution. Attempts to stimulate the ovary are very rarely successful. In the normal menopause primordial follicles vanish and ovarian atrophy takes place. F.S.H. appears in the urine and estrin, except for small quantities, vanishes. In this type of menopause estrin is of great value and in most, though not all instances, relief of symptoms is certain. The very great majority of women, however, are not troubled by the cessation of ovarian function and treatment is never sought. Only severe cases seek medical help.

The menopause as brought about by radium is caused by injury of the ovarian follicle system by the gamma rays. Primordial follicles vanish and amenorrhea occurs. Once established, this menopause is similar to that due to *x*-ray treatment. In the menopause due to Roentgen treatment the ovaries are injured from without inward. A failure of the follicle apparatus follows. The use of radium to bring about the menopause is probably best in that group of patients with any abnormal bleeding. In every instance a curettage for diagnosis should be done. If the menopause is sought for some other reason than abnormal bleeding Roentgen castration is just as good and probably is even more gentle. It is certain that abnormal discharges so often due to radium treatment do not accompany *x*-ray treated cases.

In both radiologic types of menopause recurrence of bleeding can occur. This is due to the fact that all the primordial follicles are not damaged beyond recovery and when they recover, menstruation starts again. It is not safe to assume in young women that because radium or *x*-ray has brought about amenorrhea menstruation will never occur again. If large doses are used it is unlikely, but the younger the patient the more the likelihood of a recurrence of bleeding. In an older patient who bleeds again after a radiation amenorrhea it is not fair to assume that the bleeding is benign. Investigation of the uterine cavity is essential to rule out the possibility of malignant disease which may have occurred during the phase of amenorrhea.

The surgical menopause is the most abrupt but the surest, and if a menopause is desired this is the most certain way to bring it about. Castration with removal of both ovaries used to be carried out much more frequently in the past decade than in this one. It is now believed that the ovaries are of great importance, so that when hysterectomy is performed before the age of 45, the ovaries are not disturbed and great care is taken not to injure the ovarian blood supply during the operation. In older women the ovaries are of less importance, but even in those supposedly past the menopause it is occasionally noted that hot flashes commence again after their removal. The abruptness of this menopause and the knowledge of the absence of ovaries gives certain women a very definite inferiority complex that is most difficult to overcome. Removal of ovaries in young people is to be deplored and great effort should be made to conserve ovarian tissue.

TREATMENT

The treatment of the menopause is not difficult and is usually very satisfactory. It may be carried out by means of simple sedatives, estrin, stilbestrol, progesterone, testosterone, or *x*-ray of the pituitary gland.

Sedatives such as phenobarbital, pentobarbital, and bromides may be used during the day and especially at night to assure quiet rest and sleep. In mild cases this simple treatment is effective.

Treatment with estrin is, however, the best method and large doses should be given at first to assure the patient relief from her symptoms. If this relief can be definite, even though the treatment is expensive, the patient will have faith. It is best to start patients with real symptoms with injections of 50,000 I.U. or 10,000 R.U. or 1.66 mg. of estradiol benzoate twice a week. Results may not be satisfactory for one or two weeks after commencing treatment. When relief is obtained the dose may be reduced to one injection per week and then to one-half the dose once per week, and so on. Eventually 200 to 600 units by mouth once or twice a week may suffice. It is first necessary to gain the patient's confidence, and then the dosage can be cut almost at will. Naturally the less treatment the better, but the mistake is usually made of trying to start with a low dose and working up, whereas it is better to start with a high dose and work down.

Stilbestrol, a synthetic substance which acts similarly to estrin, is of great value. It has definite side effects, such as nausea, vertigo, vomiting, etc., and is not yet accepted by the American Medical Association Council on Pharmacy and Chemistry. It is therefore not now recommended. If it is finally accepted it will soon replace extracted estrin because it is cheap and very effective, both by mouth and by subcutaneous injection.

Progestin is still too expensive to use and it is not so efficacious as estrin in the treatment of hot flashes. Occasionally it may be tried along with estrin in an attempt to produce the hormone sequence for the normal person. Estrin is used for one month and during the last two weeks of the month five injections of 5 mg. of progesterone are given every other day for seven doses. In some of the difficult cases this staggering of the two hormones is of value.

Testosterone is very effective as it is a definite inhibitor of the anterior pituitary gland and therefore depresses the secretion of F.S.H. If, as we think, F.S.H. is responsible for menopause symptoms, then inhibition by testosterone ought to be useful. It is not wise to use this hormone when others are available because of its tendency to produce masculinization. It is likely that large doses would have to be given to grow hair but it would be tragic to do this if it were not necessary. If all other methods fail it is proper to give 25 to 50 mg. per week intramuscularly for a short period of time.

X-ray of the pituitary gland is not advocated, though it undoubtedly works in some cases, since it may be dangerous. If it is necessary to check the secretion of F.S.H. to stop menopause symptoms it is quite likely that some other hormone or hormones in the gland may be depressed. Roentgen treatment of the pituitary is not recommended.

CONCLUSIONS

The menopause may be natural, or brought about by radium, Roentgen treatment, or surgery.

It is in most instances a natural phenomenon and is not attended by any real difficulties. It does cause severe symptoms in a certain percentage of women.

An increase of F.S.H. and a decrease in estrin in the urine is usually found.

There are many definite accompanying pathologic changes in the genital tract and probably balancing changes in most glands of internal secretion.

Treatment in most cases is very satisfactory and easy.

THE ROLE OF ENDOMETRIAL BIOPSY IN DIAGNOSIS

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OF critical importance to the health and efficiency of the female is the ability of the ovary to discharge its two fundamental functions, ovulation and hormone production. Thus it is that we seek diligently, and prize highly, any dependable signs of ovarian activity. At present those most easily observed are found in the endometrium.

In 1908 Hitschman and Adler[1] described the orderly progress of the endometrium from early postmenstrual proliferation to secretion or functioning, a process which terminates with the following menstruation if conception does not intervene. In 1913 Schroeder[2] suggested, and quoted Meyer as agreeing, that there was a fairly accurate time relationship between these endometrial changes and the already well known ovarian sequence, that is, the progress of the ovarian follicles from early growth through maturation, ovulation, and corpus luteum formation. Causal relationship between ovarian and endometrial changes, which Knauer[3] and also Halban[4] had postulated as early as 1900, however, had not been proved.

The female sex hormone, estrogen, was shown by Allen, Doisy and Pratt[5,6] in 1923 to come primarily from the follicles, and in 1925 also from the corpus luteum. In 1929, Corner and Willard Allen[7] isolated progestin from the corpus luteum which, in the non-pregnant, is yet its only physiologic source. It remained necessary only to prove that estrogen caused proliferation, and progestin, secretion in order to identify the follicles and the subsequent corpus luteum as the masters of the time-related cytologic changes in the endometrium. This was demonstrated in the rabbit by Corner[8] and Willard Allen[9] in 1928 and 1930, and in the macaque by Hisaw and Leonard[10] in 1930. During the next three years, Clauberg,[11] Kaufman[12] and Werner and Collier[13] showed that in the human, too, estrogen stimulated endometrial "proliferation" and presented adequate evidence that progestin evoked "secretion" or "functioning." Thus "proliferation" of the endometrium indicates that follicles, the source of the estrogen which stimulates the growth, are present in the ovary, and that "secretion" or "functioning" manifests the presence of active luteal tissue. As has been prettily said by Edward Allen, we find "inscribed on the endometrium" the record of ovarian behavior.

Unfortunately, not all the endometrium records uniformly and in a critical way, the ovarian performance. To be sure, estrogen causes all areas and layers to proliferate, but only in the superficial half do the growth changes vary significantly with the orderly development of follicles from the time they escape the inhibition of the corpus luteum phase up to the maturation of one of them. Furthermore, the specific qualities of early growth and of late growth are dependably presented only in the endometrium which lines the deeper portion of the fundus.

The same localization of typically characteristic secretory changes due to the added action of progestin on the endometrium is also recognized. Only in the superficial layers under the surface epithelium and in the adjacent glandular portion of the so-called spongy layer, and in these layers, only in the endometrium which lines the deeper half of the uterine cavity, does one find convincing evidence of combined estrogen and progestin activity.

Biopsy of these upper reaches of the endometrial field is easy and clearly reveals the inscription of the follicles and of the

corpus luteum. The method is simple. The uterine canal is first sounded to determine its direction and the nature of the internal os. A properly curved hollow cannula, not more than 3 mm. in diameter, equipped at the curved end with a sharp hood, or one with saw-toothed sides, and at the other end with a petcock, is then placed against the anterior wall high in the fundus. Suction is applied by a syringe attached to the outer end of the cannula while the hood is drawn firmly outward against the endometrium for a distance of about 1 cm. The cannula may be rotated and a similar stroke made against the posterior wall. The small petcock is then turned to close the cannula against a subsequent inrush of air as the syringe is disconnected. The cannula is withdrawn gently, and in such a way as to avoid clipping the internal os on the way out. The syringe is partially filled with fixing solution and reattached to the cannula; the petcock is opened; and the contents of the cannula are washed into a suitable bottle for fixing. Our custom has been to use a 10 per cent solution of formalin and to imbed in celloidin. Sections are cut as thin as possible, usually 14 microns thick, and stained with hematoxylin and eosin.

The criteria by which we believe one may deduce the presence of actively growing follicles, and of an active corpus luteum will be found in the descriptions which follow.

Hypoplasia. When biopsy obtains only fragments of nondescript, fragile stroma and a few small glands, which on sectioning are frequently separated from surrounding stroma, or when the curette brings forth only a long ribbon of surface epithelium with but meager bits of subjacent stroma attached, one may be sure that the production of estrogen is low, as in marked hypoplasia of the follicles with no approach to ovulation. It is a common finding in long-standing amenorrhea.

Fig. 1. Whole thickness, late secretory fundal endometrium (× 17). No function of basal portion. See Figure 2 for further magnification of inset. See Figure 3 for magnification of superficial late secretory endometrium.

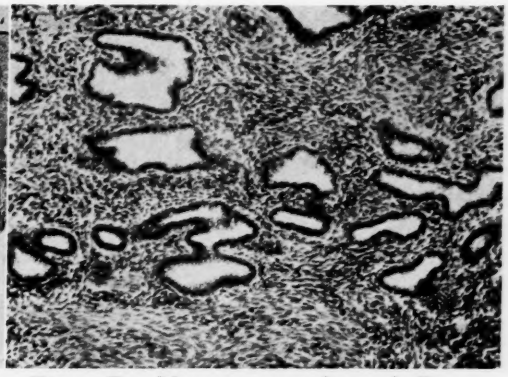

Fig. 2. Basal late secretory (× 125). Dense stroma; small chromophilic nuclei; comparatively simple glands; columnar epithelium with pseudostratification in gland epithelium. No secretion. (See Fig. 3.)

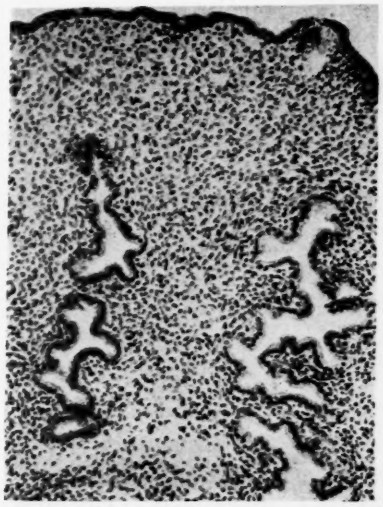

Fig. 3. Late secretory from fundal portion (× 125). Pale stroma nuclei; distorted glands; vacuolated fragmented epithelium with basal nuclei.

Early Proliferation. This is characterized by many straight glands of similar and constant caliber, usually sectioned in the same axis. These are lined by low cuboidal epithelium in which the ratio of nuclear to cytoplasmic mass is .5 or about 1 to 1. Active cell division is evidenced by a frequency of perhaps four mitotic figures in many glands. The supporting stroma is of closely packed chromophilic and practically nude nuclei.

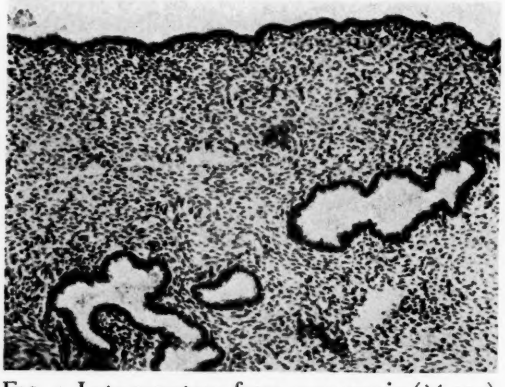

Fig. 4. Late secretory from near cervix (× 125). Small chromophilic nuclei. Pseudostratified columnar gland epithelium. No secretion.

Among these cells are many small lymphocytes, usually discrete, occasionally occurring in spheroid clumps which have been likened to lymph follicles. (These are more commonly found in more advanced proliferation.)

Though the biopsy curette removes a strip 2 to 3 mm. in thickness, there is an absence in the stroma of large irregular cavities lined by superficial epithelium so as remotely to resemble angular proliferating glands. Such units are sections of depressions in the rugous mucosa of more extensive proliferation, and their absence indicates that the endometrium is fairly smooth.

This is the cell picture drawn by the many young but actively growing follicles in a well functioning ovary during about the first six or eight days of the menstrual cycle. The similarity and simplicity of the glands, as well as the absence of sectioned endometrial valleys means that the whole tissue is but a few days old, perhaps six at the most—a condition to be found only after the orderly denudation of the decidual layers. Such uniform shedding is characteristic only of true menstruation in a previously functioning endometrium, and so bespeaks the presence of a corpus luteum in which organization is well established, a corpus luteum whose activity was associated with atresia of the older follicles in the ovary, and whose regression saw the growth of the new crop. True postovulatory menstruation occurs not as a synchronous process in all parts of the decidua, but rather in a constantly increasing number of small foci which thus gradually include the whole surface endometrium. So, if the biopsy is made while external bleeding persists, the cytology of early proliferation may be found in one focus, while section of another area may depict menstruation.

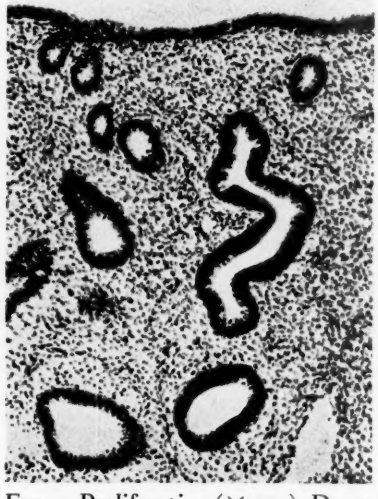

Fig. 5. Proliferative (× 125). Dense stroma. Pseudostratified gland epithelium.

Late Proliferation. This is the diagnosis when the specimen contains many sturdy, well developed glands, still of similar and fairly constant caliber, but usually sectioned in different axes, which signifies that they are slightly wavy or twisted. The gland wall is of high columnar cells in which the mass of the nucleus is to that of the cytoplasm as 1 to 2 or 3. Most characteristic is pseudostratification, i.e., the nuclei of the cells are placed at various

levels between the inner and outer borders of the epithelium. Mitotic figures occur in the luminal portion with a frequency of one or two in each of several cross sections of glands, for growth may persist until "secretion" is well established. The increase in thickness of the endometrium is accompanied by a wrinkling of its surface which permits the curette to transect it at different levels. In some places, then, the section may show only the border of a furrow between adjacent mounds. Such a depression will present in section the strangely angular lumen of what resembles a large gland lined by what might be considered atypical pseudostratified epithelium, but which is not to be confused with the lining of a gland. Such epithelium is in fact part of the surface or boundary epithelium of the mucosa. This tissue, in the human, has not yet been shown to undergo mutations characteristic of stages in the cyclical development of the endometrium.

The stroma, like that of early proliferation, is fairly dense and the cells are practically filled by the small strongly basophilic nuclei. Here and there may be seen edema, and there is almost always an occasional area containing extravasated erythrocytes. Individual lymphocytes are plentiful and so-called lymph follicles are sometimes seen. Their significance is unknown. The blood vessels are inconspicuous.

The biopsy of "late proliferation" denotes the presence in one ovary at least, of many follicles of varying ages and degrees of development, from small young follicles only 1 or 2 mm. in diameter up to several fairly large ones of a diameter of 6 to 8 mm. Such an epithelium in full flower is also found normally until several hours, doubtless twenty-four or more, after the follicle has ruptured, and so may persist for one or two, perhaps even three, days after luteinization of the theca interna has begun. If this is the case, a biopsy one week later will show the endometrium to be in the mid-secretory phase, as described below.

If menstruation occurs within ten days of the biopsy of a proliferating endometrium, one may assume it to be of the anovulatory variety, sometimes called dysfunctional uterine bleeding, for if the luteinization which evokes secretory changes is normal, it is associated soon after its inception with ovulation. Theca luteinization then normally persists and inhibits bleeding for about fifteen days from its beginning. If menstruation occurs later than the tenth day after the biopsy of a proliferating endometrium, one may only say that at the time of the biopsy there were in the ovaries some fairly mature follicles, one of which may have ruptured. If biopsies, repeated at perhaps weekly intervals, all reveal proliferating endometrium, one may say that ovulation is absent, and that the ovaries give rise to a succession of follicles which function for a time and then regress without rupture, though a few may persist as tiny cysts with little or no hormone significance.

Hyperplasia. This is an overgrown form of proliferating endometrium with essentially the same cytologic characteristics. The stroma may be exceedingly dense, the glands very numerous, and some of them may be markedly dilated—the "swiss cheese" endometrium of Novak.

The dilated glands are distinguished from sections of the mucosal "depression" described above, by their spherical shape, and their somewhat flattened epithelium. Such hyperplasia is found when follicles continuously develop and then either regress or persist, but fail to maturate with luteinization, and so to rupture. Their prolonged secretion of estrogen stimulates the overgrowth of the tissue. Intermittent bleeding may occur from such an endometrium and so nearly in cycles as to be called anovulatory menstruation. On the other hand, it may be so irregular and so variable in amount as to merit only the term "immeasurable menstruation" or "aperiodomenorrhea." The condition is still referred to as "metropathia hemorrhagica," though it is truly an ovarian and

not a metrial dystrophy. It is also called "dysfunctional uterine hemorrhage," or "uterine insufficiency."

FIG. 6. Beginning midsecretory (× 125). Diminishing edema of stroma. Beginning enlargement of stroma cells. Dilated tortuous glands; basal nuclei; supranuclear vacuolization; beginning fragmentation of cytoplasm.

Secretory Phase. Secretion or function of the endometrium is characterized by five easily identified tissue mutations: (1) *mobilization outward, then inward, of the nuclei in the epithelium of the glands;* (2) *vacuolization of this epithelium with subsequent disgorgement of the vacuoles into the lumina of the glands;* (3) *dilatation, crumpling and distortion of the glands;* (4) *stromal edema, followed by enlargement of individual stroma cells;* (5) *elaboration of the vascular tree.*

We repeat: these changes occur in some degree, throughout almost all layers of the endometrium above the basal layer, but only in the superficial portion are they consistently well marked, and only in the deeper half or two-thirds of the fundal cavity do they reach their fullest expression.

Each of the five modifications mentioned as characteristic of function develops gradually, but they overlap each other and do not appear in regimented succession. The whole process of function, however, may easily be defined in three phrases: early secretory, mid-secretory (Fig. 6), and late secretory. (Fig. 3.) The sign of the first is mobilization of the nuclei, and extends about forty-eight hours after ovulation through the next three or four days, i.e., up to about the sixth day after ovulation. The cardinal signs of the mid-secretory phase are edema of the stroma and the location of the nuclei in the base of the disgorging vacuolated cells of the gland epithelium. These two conditions appear about the sixth day after ovulation and last roughly for about four days.

The signs of the late secretory phase are enlargement of the stroma cells and increased prominence of the vascular structures. This is the period which has been characterized as showing "secretory exhaustion" (Hisaw)[14] and extends during the four days from about the tenth day after ovulation until menstruation.

The first change from proliferation is dislodgment of the nuclei from the bases of the cells in the gland epithelium, by chromophobic material which gives a basal lucid zone in sections stained with hematoxylin and eosin, and which reveals the presence of glycogen when stained with Best's carmine. This phenomenon in mild degree, is not specifically a progestin effect, for occasionally it is seen after prolonged administration of only estrogen in the castrate. It is rarely seen, too, in intact females from whom biopsies of persisting proliferating endometrium are obtained. In these women, however, it never reaches the stage of a prominently displayed lucid zone below uniformly mobilized nuclei; rather, it consists only of easily discerned vacuoles underlying the nuclei in some of the glands. As such a picture is also presented in the first stages of true progestin effect, it may cause some confusion in diagnosis. When due only to estrogen, it is commonly accompanied by other signs of disturbed hormonal reaction in the endometrium: more than normal are the variations in the quality of the glandular epithelium, in the size of the glands and in the density of the stroma.

More detailed description of the five prominent characteristics of function follows:

1. *Mobilization of the nuclei* by progestin moves them from placement at any level, as is seen during proliferation. First moving

them away from the base, it then groups them in the middle zone, and then, as they assume a common level, they are replaced in the bottoms of all cells, where they lie side by side. This change seems to transpire in not more than four days, approximately from the second to the sixth day following ovulation.

2. *Vacuolization of the gland epithelium* starts with the first mobilization of the nuclei, when the infranuclear vacuoles appear to dislodge all nuclei from the depths of the cells. As the nuclei accumulate in the midzone of contiguous cells the subjacent clear area becomes as large as, or larger than, the nuclei themselves. Apparently the material therein migrates centrally as the nuclei settle back to the bottom, for numerous large thin walled vacuoles appear in the cytoplasm superficial to the nuclei when these become uniformly basal. When vacuoles appear thus, throughout the supranuclear cytoplasm, the luminal border of the cell becomes frayed by their rupture. Their disgorgement continues with increasing mutilation of the cell wall and depletion of the cytoplasmic mass until finally what began as high cylindrical cells become pseudocuboidal. This process of preliminary mobilization of nuclei and subsequent depletion of the cells takes place from about the second to the fourteenth days after ovulation.

3. *Dilatation of thoroughly proliferated glands* is seen when the central surface of the epithelium becomes frayed by the evacuation of vacuoles about the sixth postovulatory day. One or two days before this the swelling of the individual epithelial cells causes a *crumpling of the glands* which forces them to assume a wavy or twisted course through the stroma, and each gland to be possibly sectioned in several different planes. As dilatation progresses, this crumpling becomes more marked and the glands become more tortuous, so that by the tenth postovulatory day, a cross section of tissue reveals lumina of various shapes and sizes, bounded by vacuolated epithelium lying in folds or in a so-called "saw-toothed" layer. Such is the picture during the week preceding catamenia, when an organizing corpus luteum is present in an ovary.

4. *Edema of the stroma*, though appearing in slight degree in small disjointed areas of the endometrium during proliferation, becomes uniform throughout the functional layers, and extreme in amount, during the twenty-four to forty-eight hours of about the sixth to the eighth days following ovulation, after which time it gradually diminishes. The stroma nuclei are then seen connected to one another by only thin strands of cytoplasm over spaces of perhaps five to ten times their diameter. As the edema increases, the stroma nuclei enlarge and become somewhat less chromophilic. Most striking, however, after the peak of the edema and while it subsides, is the accumulation of cytoplasm in the cells, first in the vicinity of the arterioles, then alongside the glands, and just under the superficial epithelium, and finally throughout the tissue above the lower half of the spongy layer. These large, pale staining, finally contiguous stroma cells form what has been termed the predeciduum. The transformation occurs during the five days preceding menstruation, or from about the ninth to the fourteenth days after ovulation.

5. *Elaboration of the vascular tree* consists of a marked growth of each spiral arteriole, and an increase in the number of its terminal capillaries. When edema is extensive, the arterioles become prominent. As the edema subsides their walls are seen to be thicker, and as the adjacent stroma cells increase in size, the arteriole is found to be sectioned in more places, an evidence of increased tortuosity. The capillaries too are seen as a freely branching network in the area just under the superficial epithelium. This proliferation of the vascular system which may have begun earlier, but was obscured until edema dissected the tissue, becomes noticeable about five days before menstruation, or when the ovum is about nine days old. During the succeeding

days, individual arterioles when sectioned appear in groups of very thick walled transected loops or short segments.

Fig. 7. Postovulatory menstruation (× 125). Disruption of tissue; depleted gland epithelium with basal nuclei.

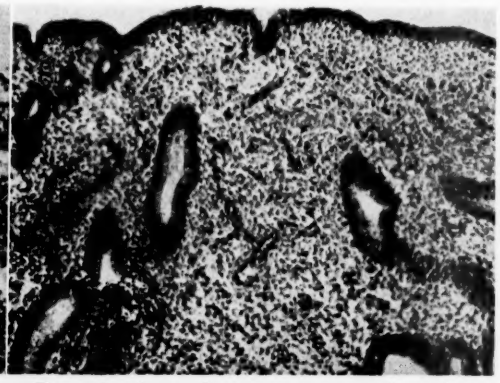

Fig. 8. Anovulatory menstruation (× 125). Disruption of tissue with necrosis of cells; glandular epithelium is high columnar and pseudostratified.

Postovulatory Menstruation. In biopsy material the process which will end in disintegration of the mucosa is seen to begin from twenty-four to forty-eight hours before disruption of the binding epithelium releases red blood into the fundal cavity. The actual process starts in isolated foci as an infiltration of the solid decidua-like superficial layer by an increased number of lymphocytes and polymorphonuclear leucocytes. The former are seen as discrete cells sprinkled freely in the tissue; the latter in smaller numbers are seen in migratory form as they are caught squeezing between the large contiguous stroma cells. The spiral arterioles are prominent but neither consistently filled nor empty, for they may be either. The capillaries, too, are sometime seen engorged with erythrocytes, in other sections, collapsed. When menstruation is but twelve to twenty-four hours distant, we find, in addition to the white cell infiltration, masses of erythrocytes free in the predeciduum, just under the superficial epithelium which is occasionally seen to be already separated from its attachment to the stroma, though still intact. When menstruation is imminent or already recently established, this extravasated blood is distributed freely in small clumps throughout the tissue, and in some places the superficial epithelium, lifted from its stromal base, may be broken to allow red blood to stream outward. When we see marked leucocytic infiltration of decidua-like tissue, containing large irregular glands with vacuolated or cuboidal epithelium, we may be sure that progestin has been active for many days, and that catamenia is at hand. A follicle with partially organized coagulum, and a thick layer of lutein cells is uniformly found in the ovary in such a case; all of which bespeaks ovulation about fourteen days before.

Anovulatory Menstruation. Biopsy may reveal hemogenic disruption of a stroma which consists of the small chromophilic comparatively nude nuclei, and which surrounds the comparatively straight or gently waving glands with pseudostratified epithelium which are characteristic of a proliferative endometrium. This means shedding of a mucosa which has been subjected only to estrogen. In such cases, though menstruation is beginning, we say ovulation has not occurred, only because there has been present no corpus luteum to supply progestin sufficient to evoke the missing functional changes described above. Frequently in proliferated endometrium we see a generous infiltration of lymphocytes. This is not prognostic of flow as is the case when the completely developed predeciduum is freely invaded. At present there is no recognized cytologic sign of impending flow from a proliferative

endometrium, except gross extravasation of erythrocytes with disintegration of the stroma. Following such a biopsy there is always staining at least, and usually flow. Whether this flow would have occurred without the preceding biopsy one cannot say. Because the same quality of atypical flow occurs frequently a long time after biopsy, we may assume that the bleeding is often hormonologic and not traumatic.

Endometritis. When polymorphonuclear leucocytes are seen in appreciable numbers in the stroma, and, massed with lymphocytes or perhaps plasma cells and debris, in the lumina of the glands, inflammation is present. In menstruating women such inflammation is almost always chronic. Such a diagnosis should not be made when only the rather profuse but physiologic infiltration of lymphocytes is seen in proliferative tissue; nor must the similarly physiologic invasion of the late secretory and sometimes the late proliferating endometrium by lymphocytes and polymorphonuclear leucocytes be interpreted as inflammatory. Such mobilization of neutrophiles precedes the diapedesis of the erythrocytes which will eventually dissolve the tissue into fragments and precipitate menstruation.

DISCUSSION

How accurately do the cytologic qualities of the endometrium reflect the condition of the ovarian follicular system? The author believes they do so to a high degree of probability only, which may also be said of most diagnostic procedures. Greater accuracy waits on more extensive and numerous correlated observations, but especially on further insight into the physiology of the two tissues themselves, the endometrium and the follicles. Of the former, we know little beyond its anatomy and that progressive changes therein are brought about by estrogen and progestin, acting on the glandular epithelium, the stroma and the vascular system. Of the follicles too, we know only little more than their anatomic, and to a slight degree, their hormonologic qualities. We credit them with the production of estrogen, and to the matured form of usually only one of them each month, the corpus luteum, we attribute the production of the two hormones, estrogen and progestin. As these hormones evoke the endometrial mutations described above, so vice versa, these mutations reflect the growth of the follicles.

For the correct diagnosis of deviation from normal menstrual behavior, biopsy is of great service, and will be of increased value to the clinician when substances are isolated which will affect the germinal epithelium, either directly or through the anterior hypophysis. By reference to the endometrial condition we may learn whether immature or persisting follicles, secreting estrogen, are present or not. We may also tell whether luteal tissue is functioning; and, within the fairly narrow limits of plus or minus two days, just how long the endometrium has been subjected to the joint action of estrogen and progestin. Study already seems to show that, normally, secreting luteinized cells are active for about sixteen days. We believe too, that shortly, perhaps twenty-four to forty-eight hours after luteinization begins, the follicle normally ruptures and releases the ovum. The period from this time to normal menstruation seems fixed at about fourteen days with a remarkable definiteness, and during these days the endometrium changes progressively.

In the absence of pregnancy, the endometrium may confidently be expected to deciduate on about the fourteenth day after ovulation. Exceedingly rare cases of regression of a progestinized endometrium without flow, such as is the rule in subprimate mammals, have been observed, but as far as the author knows, not formally reported. He has himself seen one case among more than 1000, and has heard of two more. They are not to be expected. The absence of flow between a biopsy showing secretion and a subsequent one showing proliferation would discover such atavism.

By biopsy then, we may tell whether ovulation occurs and tell approximately how many days have elapsed since ovulation, and in how many more days normal menstruation should begin. If breakdown of the endometrium occurs much before the estimated date, we may safely infer a disturbance in hormonal balance which may have profound implication with fertility, for it signifies either a fault in corpus luteum physiology or in the little understood menstrual urge.

This distinction will become very important as pharmaceutic hormone preparations, which will affect either, become available. Already progesterone in repeated doses of 5 to 10 mg. may delay the destruction of the predeciduum, and estrogen in fairly large daily doses of 2000 or 3000 units may inhibit ovulation and corpus luteum formation. In smaller doses, of 1000 units or less, estrogen may be expected to stimulate corpus luteum formation and activity, probably by way of the anterior pituitary, or directly to support a functioning corpus luteum as has been shown in the hypophysectomized rabbit (Robson[15]). Rationally to plan hormone treatment of the female reproductive system and to estimate its effectiveness, biopsy of the endometrium is of great aid.

For correct interpretation of biopsy evidence it is usually necessary to make the examination with careful reference to periods of uterine bleeding, and especially to that flow which succeeds the biopsy. It is sometimes profitable to repeat biopsy at weekly intervals. Especially in the examination of patients complaining of infertility, and in others as well, caution must be exercised that abortion be not unconsciously perpetrated. In sterility work some prefer to perform the biopsy only during the first few hours after the beginning of menstruation. Gratifying has been the unusual induction of pregnancy apparently by biopsy performed during the postovulatory phase. This the author has seen in four cases. All had been inexplicably and involuntarily barren for at least two years. They all skipped the period which was expected within a week of the biopsy. The fertilized ovum must have been present in all of them when the biopsy was made. Explanation is necessarily limited to theory.

The discovery in our clinic of four cases of unsuspected tuberculous endometritis contributes to the advisability of frequent, if not routine, biopsy examination of the endometrium.

SUMMARY

Since the cytologic pattern of the endometrium is specifically affected by the follicular hormones, examination of the endometrium will discover the condition of the follicular system in so far as it has hormonological activity.

The effect of estrogen and progestin is most characteristic in the superficial layers of the endometrium and in that portion of the mucosa which lines the deeper half of the fundal cavity.

Biopsy is made with an appropriate cannula by scratch with suction.

The criteria for identification of estrogen and progestin effects are given in detail. The signs of their single or joint quantitative effect, and to some extent of its duration, are expressed in the common diagnoses, hypoplasia, hyperplasia, proliferation, secretion, true menstruation and anovulatory menstruation.

Biopsy is shown to be of great assistance in the diagnosis of menstrual disturbances, in the recognition of ovulation, and for the rational use of pharmaceutic hormones and for the evaluation of their effect. It is, incidentally, of help in the detection of unsuspected tuberculous endometritis.

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NEWER ASPECTS OF DIAGNOSIS IN EARLY CARCINOMA OF THE CERVIX UTERI

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PORTLAND, OREGON

AS the title indicates, this discussion will be limited to methods for recognizing early cancer of the cervix uteri. This also necessitates a consideration of some borderline lesions that are not frankly cancer. These areas of non-invasive carcinomatoid change are still generally recognized by the rather misleading and often misinterpreted term, precancerous, and are regarded unequivocally by some as forerunners of bonafide cancer.

We have all had the too frequent experience of observing patients who have a history of some type of bloody or malodorous vaginal discharge that has existed for months and who possess an obvious, advanced cancer when they first consult their physician. These individuals generally do not represent diagnostic problems and here the physician's responsibility in making an early diagnosis is minimal, for frequently such patients delay seeking advice not solely because of ignorance but from fear. However, even in such apparently obvious and advanced processes, it should be axiomatic that a diagnosis of cancer is never acceptable without verification by removal of tissue for biopsy.

It is true that advanced cancer of the vaginal portion of the cervix (portio vaginalis cervicis) appears as an ulcerating, friable and generally firm process of varying size, and as a general proposition it can be recognized by its gross appearance. Therefore, before one is expected to recognize cancer in its early stage, one may reasonably inquire what there is about such an obvious and well developed cancer that grossly characterizes it. The answer, heretical as it may sound, is that advanced cancer probably possesses no distinctive or grossly pathognostic appearance. Its clinical recognition rests on the mere coincidence that most ulcerating, indurated tumors of the portio are cancer. However, occasionally such a lesion may prove to be the evidence of syphilis, tuberculosis or more rarely venereal granuloma. The reason for histologic confirmation of the clinical diagnosis is therefore obvious.

Early cancer of the cervix, merely for the purpose of clarifying the discussion, may be considered under two categories: (1) that phase where the cancer, while still small, is clinically recognizable; (2) an earlier phase in which one is not ordinarily prepared to recognize it and the gross physical aspect of the tumor is not so apparent. For descriptive purposes the latter may be considered as hidden, covert or, possibly, clinically latent cancer.

Clinically recognizable early cancer of the vaginal portion of the cervix, as physicians have been taught to recognize it, usually presents itself as a red, firm, irregular, somewhat elevated circumscribed process, situated ordinarily in the neighborhood of the external os. It generally bleeds readily on light manipulation with a soft cotton pledget and on palpation may feel indurated, although induration as a highly diagnostic sign has probably been overemphasized. It is a lesion that should at once arouse one's suspicion as to its malignant character.

The primary prerequisites for its recognition are: adequate exposure of the cervix; adequate illumination; and deliberate, thoughtful inspection. The value of the colposcope in studying such a lesion will be discussed later. There is little doubt that, if all physicians would observe these elementary requirements, most cervical cancers would be suspected on the first examination while they were still comparatively

early and yet advanced far enough to produce slight tumefaction, a small ulcer or some other superficial change outside the normal variation, although symptoms might be entirely lacking. Obtaining tissue for histologic examination without undue delay is imperative, to establish the diagnosis and advise treatment. Especially important is it that until an adequate histologic study has been made, all attempts at treatment of such suspicious areas be withheld.

The lesion which according to my experience is most commonly suspected of being an early cancer is the vermilion zone so commonly observed about the external os. This, generally referred to as an "erosion" or "ulceration," has a well marked tendency to bleed when complicated by vaginal inflammation, which renders the red surface especially susceptible to slight trauma, with the production of minute bleeding points (erosions). Generally, however, the circumostial vermilion zone does not bleed and does not partake of the nature of erosion or ulcer.

The differentiation of a circumostial vermilion zone of altered epithelization from an established cancer of similar size should ordinarily not be difficult. The former may be relatively smooth and flat or it may possess a fine irregularity giving it a finely granular appearance. It does not, however, appreciably change the gross contour of the cervix. If it involves both lips of the cervix, as it often does, it has its greatest expanse on the anterior and posterior lips, with narrow lateral connecting zones of red. On palpation with a sound the surfaces are found to be elastic, and under magnification cervical glands visibly pour forth their watery secretion onto an intact, red and glistening mucosa.

A small carcinoma on the surface of the portio does not have as perfect a circumostial distribution as the common vermilion zone does, and ordinarily it is elevated, so that it alters the contour of the cervix. Its color generally offers a distinct contrast to the surrounding mucosa, while its surface is usually irregular and may show the opening of cervical glands. Palpation of the tumor with a sound, especially under magnification with a colposcope, reveals the irregularity previously noted and a lack of elasticity. If there is beginning degeneration of the tumor the sound can be pushed with little force into the substance of the tumor, which then bleeds readily.

A small cancer with ulceration can so simulate a benign, nonspecific, inflammatory process of the cervix, while a benign process when complicated by induration and bleeding can so mimic cancer, that their gross differentiation may be impossible. However, such instances have so far been relatively uncommon.

In summary, early cancer of the vaginal portion of the cervix that is clinically recognizable, as ordinarily encountered, presents a gross appearance which shows sufficient deviation from the normal to arouse suspicion. Obviously, its true nature may not be recognized. Nevertheless, thoughtful appraisal of the lesion on the first examination should arouse sufficient concern to stimulate the proper removal of tissue for histologic study.

COVERT CANCER

We come now to a consideration of those processes on the vaginal portion of the cervix which, though their appearance does not correspond to the customary gross appearance of cancer, may represent, as we have noted elsewhere,[1] an early phase of malignant change, i.e., covert cancer. Until comparatively recently such processes have been detected accidentally on laboratory examination and have been unrecognized clinically as either potential or bona fide early, nonulcerating cancer.

The attempt has been made to bridge the hiatus between the phase of early tumefaction and ulceration of cancer and the antecedent covert stage, in which these changes have not occurred.

Despite much effort and many reports concerning the recognition of covert cancer, instances where bona fide cancer prior

to the stage of ulceration or tumefaction was suspected clinically and verified histologically are not common. Cases reported by Haselhorst[2] and Marti[17] are possibly such examples. Attention has been focused on these areas and other areas of a more controversial character by Hinselmann[3] and by Schiller.[4,5] Generally such an area on examination with a speculum appears as a white, opaque, sometimes slightly wrinkled plaque, which may appear somewhat raised, of varying size (usually small), which is termed a leucoplakia. It is believed by some that cancer of the cervix in its earliest grossly recognizable form reveals itself as a leucoplakia (white spot). The problem would be simple if this were the entire story. However, when one enters into a discussion of leucoplakias which are considered cancerous because their epithelium shows a superficial carcinomatoid change, one becomes involved in the vexatious question of how to recognize histologically that such an area is truly an incipient cancer and therefore destined to become invasive. Obviously, this is a problem with which the practicing physician does not ordinarily have to concern himself since he feels that is the pathologist's problem. However, if the practicing physician is to concern himself with the matter of detecting covert cancer and the methods proposed for accomplishing this, he must have some appreciation of the problem involved or he will find himself faced by one dilemma after another. Our discussion of this will be brief since it concerns those non-invasive carcinomatoid changes in the cervical epithelium which are recognized by such terms as precancerous, cancer in situ, probable beginning cancer, intraepithelial cancer, Bowen's disease, non-invasive potential carcinoma, etc.

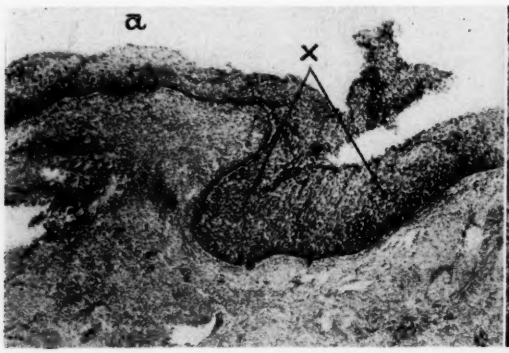

Fig. 1. Illustrates the epithelial change that may occur at the margin of a bona fide cancer. At *a* the epithelium is essentially normal while at *x* it has all the histologic characteristics of cancer but without invasion. (From Martzloff, in *Bull. Johns Hopkins Hosp.*, 33: 221, 1922.)

Fig. 2. From same specimen as Figure 1. *a*, the cervical canal; *b*, a club-shaped mass of cells histologically identical with cells at *x* in Figure 1; *c*, clumps of cancer cells in lymphatic spaces. Figures 1 and 2 illustrate the necessity of adequate tissue for histologic study if a proper differentiation is to be made between an early cancer such as this and a lesion showing only "non-invasive carcinomatoid change" as illustrated by Figure 3. (From Martzloff, in *Bull. Johns Hopkins Hosp.*, 33: 221, 1922.)

In short, cancer of the vaginal portion of the cervix in its incipiency is *assumed* to pass through a stage in which the cells of the stratified epithelium in a given area possess all the histologic earmarks of cancer but lack the property of invasion.

Laying aside all theoretic considerations, one cannot say positively whether the ultimate fate of such suspicious lesions after a varying period of latency will be one of steady progression to invasion and full-blown malignancy or whether there may occur a process of regression and restitution to normal. Similar epithelial changes are occasionally found at the periphery of bona fide cancers, and it is therefore necessary when the histologic picture of a

non-invasive carcinomatoid change is seen to make certain that the material has not come from the margin of a full-blown malignant process.

In practical application, the instances of covert cancer so far reported, with few exceptions, fall into this group showing non-invasive carcinomatoid change. Since some observers consider such areas as bona fide local cancers, therefore possessing the power of ultimate destructive invasion, it appeared logically imperative to develop some means for their detection at a time when ulceration or tumefaction were absent.

Methods for Revealing Areas of Abnormal Epithelial Change. Two methods to solve the problem have been proposed almost simultaneously. Both have for their ultimate aim to render visible the areas under consideration, but the procedures used to bring this about are fundamentally different.

The first is the *iodine test* proposed by Schiller to study the tinctorial reaction of the stratified epithelium of the vaginal portion of the cervix. The rationale underlying this test, which is described in the next paragraph, is based on the observation of Lahm, Schiller and others that histologic preparations of cancerous epithelium when stained for glycogen usually show it as absent. Langhans has shown that glycogen in living tissue stains with iodine. Using this observation Schiller has been able to demonstrate that the cells belonging to areas of non-invasive carcinomatoid change as well as the grossly normal, but cytologically cancerous epithelium that surrounds some well established cancers does not give the dark brown color reaction as does normal epithelium. The difference in the staining reaction between the two types of intact epithelium offers a sharp and visible contrast which the alert examiner cannot easily overlook.

The iodine test is done as follows: The cervix is exposed as in any speculum examination and excessive secretion is gently wiped away with cotton. A cotton pledget dripping with Gram's iodine solution (iodine 1 part, potassium iodide 2 parts, water 300) is applied repeatedly to the cervix until it takes on a deep chestnut brown color. It requires several seconds for the color to develop. Pathologic epithelial areas, in particular cancer epithelium, according to Schiller, take no stain or at most assume a faint yellow color and therefore stand out in distinct relief. The iodine solution should be comparatively fresh.

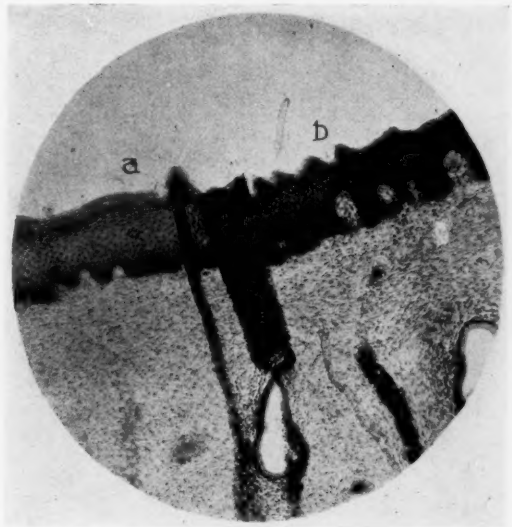

Fig. 3. From a cervical polyp. *a*, essentially normal stratified cervical epithelium, while at *b*, the epithelium has undergone a profound and abrupt change. Here the cells are irregular in size, shape and staining reaction, layer formation is lost and from three to five mitotic figures may be seen in some high power fields. This is a typical example of non-invasive carcinomatoid change (so-called superficial cancer, precancerous lesion, etc.). This area is small, circumscribed and no invasion is demonstrable. Otherwise its appearance is as typical of cancer as the cancerous areas in Figures 1 and 2. Some leucoplakiae possess a similar histologic structure. (From Martzloff, in Dean Lewis' Practice of Surgery, Prior.)

The other method depends on the use of the colposcope. This was devised by Hinselmann as a result of his observation of two large areas of leucoplakia (white plaques) on the vaginal portion of the cervix. Histologically these areas showed the cellular changes ascribed to cancer (mitoses, irregularity in size, shape, relationship and staining reaction of the cells), but they were limited to the anatomic

confines of the epithelial zone, i.e., invasion was lacking. On the basis of this observation and a few earlier observations by von Franqué and others, which have been discussed elsewhere,[6] it appeared reasonable to infer that leucoplakia offered a starting point for cancer. Indeed, it has long been held by von Franqué[7] that cancer of the portio probably manifests itself first as a leucoplakic change and, conversely, that certain leucoplakic plaques are destined eventually to become cancers. It therefore appeared logical to attempt to recognize these changes in their incipience when they might be so small as to escape observation by the unaided eye. The magnification from 10 to 15 diameters which the colposcope provides is designed to make such recognition possible and also to permit study of lesions other than leucoplakia.

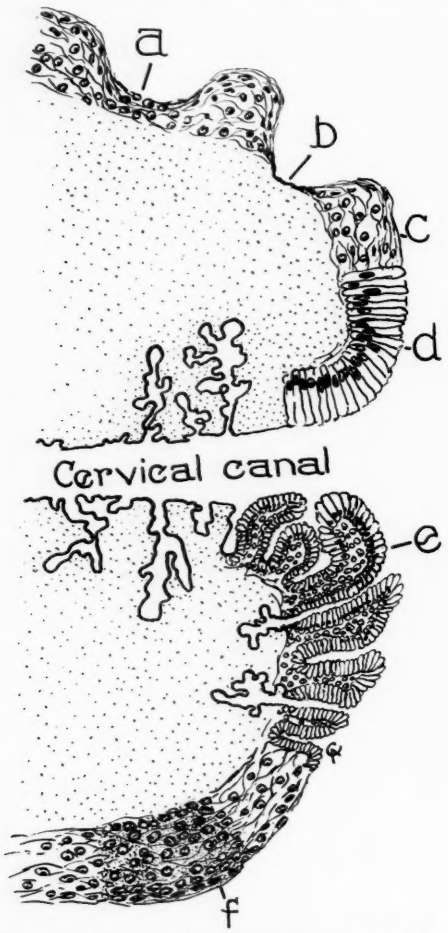

FIG. 4. Schematic representation of the portio vaginalis cervicis to show some of the types of areas that react differently to the iodine test. *a*, superficial erosion that does not stain. *b*, a deep erosion or small ulcer that may take a brown or modified brown color. *c*, normal stratified epithelium which stains mahogany brown. *d*, columnar epithelium that has grown out from the cervical canal on to the portio to produce the familiar vermilion zone about the external os which retains its red color just as does area *e* with the iodine stain. *e* is frequently and incorrectly termed a papillary erosion, but differs from *d* only in that it has a papillary structure. *f*, an area of non-invasive carcinomatoid change or a leucoplakia which does not stain. (From Martzloff, in *Internat. Clin.*, 4: 179, 1934.)

Study of the cervix under magnification is interesting and informative if one controls one's observations with histologic studies. One learns that the cervix generally has a slight but definite pulsation synchronous with the heart beat; that cervical glands may open onto the portio 1 or 2 cm. from the external os through a normal, stratified epithelium, which is bathed by their intermittent, crystal-clear secretion, and that gland openings commonly occur also in the circumostial vermilion zone and may have there small yellowish gray plugs simulating leucoplakia. Also it is not uncommon to note at the transition zone, where the pale pink of the normal stratified epithelium meets the bright red of the thin epithelium of the vermilion zone, areas where the epithelium is pale gray, almost white. Minute bleeding points (erosions) and small ulcers can be readily identified, as can also other more major deviations from the normal.

Results of Tests. The question naturally arises as to how valuable these two methods are for the recognition of incipient cancer or areas of non-invasive carcinomatoid change, when compared with ordinary methods of careful inspection.

Our experience with these methods now extends over approximately nine years. Unquestionably the iodine test is not specific for cancer or for areas of so-called non-invasive carcinomatoid change. Schiller originally pointed out some of the pitfalls in this test, but felt that nonstain-

ing areas are often, though not always, cancerous. According to our experience the overwhelming majority of unstained areas, including areas of leucoplakia, shows no histologic evidence suggestive of a non-invasive carcinomatoid change. Small epithelial gland plugs, vermilion areas, a proportion of superficially situated Nabothian follicle cysts, areas of epithelial loss, either when superficial or, if complete, apparently when fibrin covers the base of the ulcer, epithelium involved in an underlying inflammatory process and particles of adherent inspissated secretion, together with other unexplained areas, fail to stain with the iodine. It follows that if areas that do not stain with iodine are not interpreted with due reserve they lead to endless confusion and alarm for the physician and unnecessary removal of tissue for biopsy, cervical tinkering and hysteria for the patient.

Up to the present time I have not discovered a histologically proved area of non-invasive carcinomatoid change with the iodine test, nor has the test, which is used routinely, so far proved to be of any more assistance than careful inspection with the unaided eye.

The altered epithelium that does not stain with iodine which occurs at the periphery of some established carcinomas has, as in Henriksen's case,[8] occasionally led to the suspicion and recognition of a cancer. So far, however, in most of such published instances[9] a history of bleeding and an ulcerating cancer were present which should have caused suspicion from the beginning. It is probably permissible to conclude that in its general application a test as unspecific as the negative iodine reaction is likely to be more confusing than helpful. Certainly, as has been noted elsewhere,[10,11] the test is not pathognomonic of a malignant condition, though it may possibly be a signal which calls for further study.

The colposcope, since it facilitates visual observation of the cervix uteri, would naturally appear to answer an unfulfilled need and to fall into the category of nasal and aural specula, the proctoscope and the cystoscope. However, the comparison is not so apt as it sounds, for from the standpoint of the profession at large it has several drawbacks which probably will prevent its general adoption. These include the expense of the instrument, the time necessary to make a careful study and the need of extended experience to interpret correctly what one sees. The need of extended experience makes it necessary for the clinician to use the instrument regularly and to correlate the colposcopic appearance of the cervix with the histologic picture of the area in question. This requires frequent diagnostic section and study of the tissue by the clinician himself. The obtaining of tissue for biopsy takes the method out of the realm of simple non-technical procedure, for if an area is sufficiently abnormal in appearance to warrant removal of tissue, removal should be carried out as described later. An

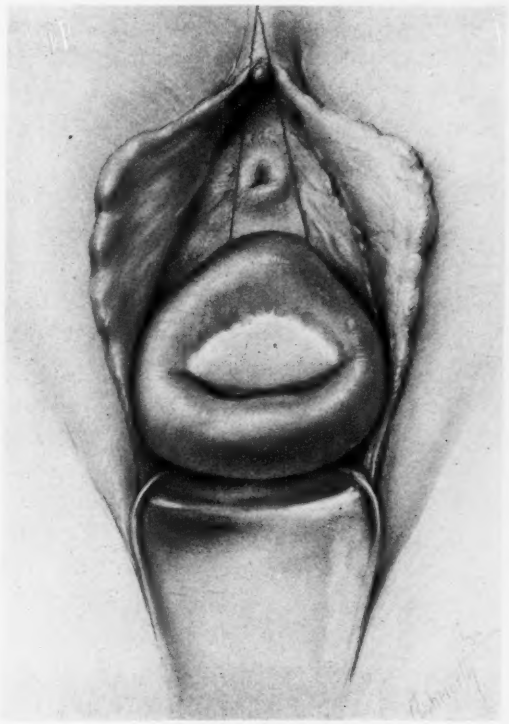

Fig. 5. A leucoplakia involving anterior cervix at external os and extending into canal. Histologic study revealed nothing noteworthy except a superficial stratum corneum.

inadequate specimen for biopsy is probably worse than none, for it frequently makes it impossible for the pathologist to arrive at a correct interpretation. If cancer is present and the specimen does not contain any of it the patient's welfare is unjustifiably jeopardized.

The colposcope, since it aids in inspection, is a fundamental contribution to methods of visual examination of the vaginal portion of the cervix uteri. While we use it as a routine, it has been of essential value in only a few instances. So far we have discovered with it neither areas of unmistakable non-invasive carcinomatoid change, non-ulcerating (covert) cancer, nor any small cancerous ulcers which could not be detected with the unaided eye on careful methodical examination. It is important to appreciate fully that the gross appearance of the small lesion of early established cancer, as pointed out by Hinselmann,[12] is not sufficiently characteristic to permit its differentiation from other nonmalignant lesions solely on the basis of its appearance through the colposcope.

The impression therefore is inescapable that for the present the recognition of cancer of the cervix uteri in its early stages still rests on painstaking visualization and inspection and proper obtainment from unusual appearing areas of tissue for microscopic examination. To await the appearance of a large ulcer formation, obvious induration or a cauliflower-like tumefaction such as that described in textbooks before clinically suspecting cancer is like preparing for sea after the ship has sailed.

This critical evaluation of methods more or less recently popularized for the apparent simplification and ready determination of early cervical cancer should not be construed as unfriendly criticism, for there are those who are enthusiastic concerning their value.[13–16] However, as noted before, on the basis of a fairly long and appreciable experience we agree with those[17–19] who believe that these methods possess greater limitations than are ordinarily ascribed to them.

ENDOCERVICAL CANCER

So far our discussion has concerned itself solely with cancer arising on the vaginal portion of the cervix. Obviously early cancer arising in and still confined to the cervical canal does not lend itself to the same methods of detection as do similar lesions on the portio. Endocervical cancer is therefore generally unsuspected and undetected until it gives rise to symptoms which are almost without exception due to a breaking down of tumor tissue. This ordinarily produces some type of bloody discharge which may or may not be malodorous. A small bit of cancer epithelium may plug the cervical canal long enough to produce a small pyometra which, when it finally expels the friable cancerous obstruction, produces a sudden, copious gush of malodorous secretion which is the first sign of mischief. Obviously inspection of the cervix when the cancer is small and well within the canal is irrelevant and the presence of a malodorous blood tinged discharge is certainly not diagnostic of cancer, although it should be so considered until it is proved otherwise. The sudden copious discharge of pent-up secretion is, of course, practically pathognostic of a cervical obstruction which may be benign or malignant.

Naturally when an occult endocervical cancer is suspected, as a matter of routine, the entire uterine cavity should be regarded with misgiving until proper study has fixed the type and site of pathologic change. The problem of diagnosing suspected endocervical cancer is considerably more difficult technically than that presented by a suspicious nonsymptomatic area on the portio which has been discovered possibly with the aid of the iodine test or the colposcope. This is because an endocervical cancer when it first produces symptoms may be early or well advanced, but it is generally complicated by infection. If a pyometra is present immediate extensive manipulation is contraindicated.

Procedure for Routine Study to Detect Early Asymptomatic Cervical Cancer. The

clinical methods we have described for detection of areas suspicious of early cervical cancer are applicable only to the vaginal aspect of the cervix, and in the course of such a survey an early asymptomatic endocervical cancer may be overlooked. In order to try and avoid this oversight it is advisable to employ a definite routine somewhat as follows:

1. Customary bimanual abdominovaginal and abdominovaginorectal examination. We generally do this after the speculum examination.

2. Meticulous examination of the vagina and cervix through a speculum. For this the patient should be in the lithotomy position and adequate illumination obtained either with a head mirror or an illuminated speculum.

(*a*) Colposcopic study of the cervix (optional).

(*b*) Staining reaction of the cervix to Gram's iodine solution (optional).

(*c*) Exploration of the endocervix.

The most distal portion of the endocervix, if the external os is large enough to permit it, is inspected by separating the lips with long tissue forceps or other suitable instrument. In this way in favorable instances the lower 1 or 2 cm. of the cervical canal may be clearly visualized.

A small sound is then passed the entire length of the cervical canal after the cervix has been cleansed and a suitable antiseptic applied. This maneuver will reveal among other things an unsuspected stricture and friable tissue, if present in sufficient amount. If bleeding follows this type of cervical exploration and no definite stricture or friable tissue is detected, 10 per cent silver nitrate may be applied to the cervical canal and the patient asked to return in five to seven days. Such bleeding generally is not due to cancer. On the subsequent visit, the canal is once more explored with a sound. If bleeding again occurs a special small, narrow, sharp curette may be gently employed to remove any tissue that comes away with light pressure. This is immediately fixed in 10 per cent formalin and used for microscopic study. Obviously a supravaginal hysterectomy should not be done closely after this type of procedure.

When bleeding occurs and one is suspicious of friable endocervical tissue at the time of the first cervical exploration with the sound, further study should not be done until proper operating room and laboratory facilities are available.

Whether the area suspected of possible malignancy lies on the vaginal portion of the cervix, within the cervical canal, or both, one is immediately confronted with the necessity of obtaining tissue for biopsy.

BIOPSY

Here again our discussion is concerned solely with the problem of obtaining tissue for diagnosis from suspicious areas that may harbor either *bona fide* covert cancer or areas that represent a non-invasive carcinomatoid change. The matter of obtaining tissue for biopsy under these circumstances becomes one of real importance, for unless the tissue is adequate and properly obtained, it may be impossible to have sufficient material on which to base a diagnosis. Particularly true is this when there is a question whether a given lesion represents a bona fide malignancy or merely a non-invasive carcinomatoid change.

No hard and fast rules can be laid down for obtaining tissue for biopsy in each variety of lesion. Only broad general principles can be indicated. Most pathologists can testify to personal experience with tissue submitted to them from cancer-afflicted patients which either showed no cancer or was of debatable character while full-blown carcinoma existed a few millimeters from the site of the specimen. Tissue removed from a small circumscribed area suggestive of cancer should include both material from the suspicious area and a generous amount of adjoining normal-appearing tissue. The block so obtained should be rectangular or nearly so, as shown in Figure 9, and should immediately

be fixed in solution of formaldehyde or other suitable fixing solution. If the material is obtained and prepared in this way, when it is ready for microsectioning there is little doubt about the direction in which the block should be cut. Minute fragments of tissue, wedgeshaped pieces of tissue and material obtained by scooping out tissue with the endothermy loop may be entirely unsatisfactory. The advisability of curetting the surface of the process as has been recommended is also a dubious procedure. Ordinarily there can be little excuse for such haphazard methods when the lesion is small, circumscribed and primarily a diagnostic problem.

When the area under suspicion is more diffuse, extends into the cervical canal, or is located on a cervix that otherwise merits some form of operative correction, an amputation or preferably a Sturmdorf procedure combined with amputation, as described by Te Linde,[20] is a convenient method of simultaneously obtaining material for biopsy and correcting a local pathologic condition. Whether the scalpel or the endothermy current is employed for this purpose probably matters little. However, if the latter is used one should allow for destruction by heat along the margins, where the fragment of tissue becomes unsuitable for histologic study. When a tumor is large and its character obvious, naturally observance of such minutiae is not essential.

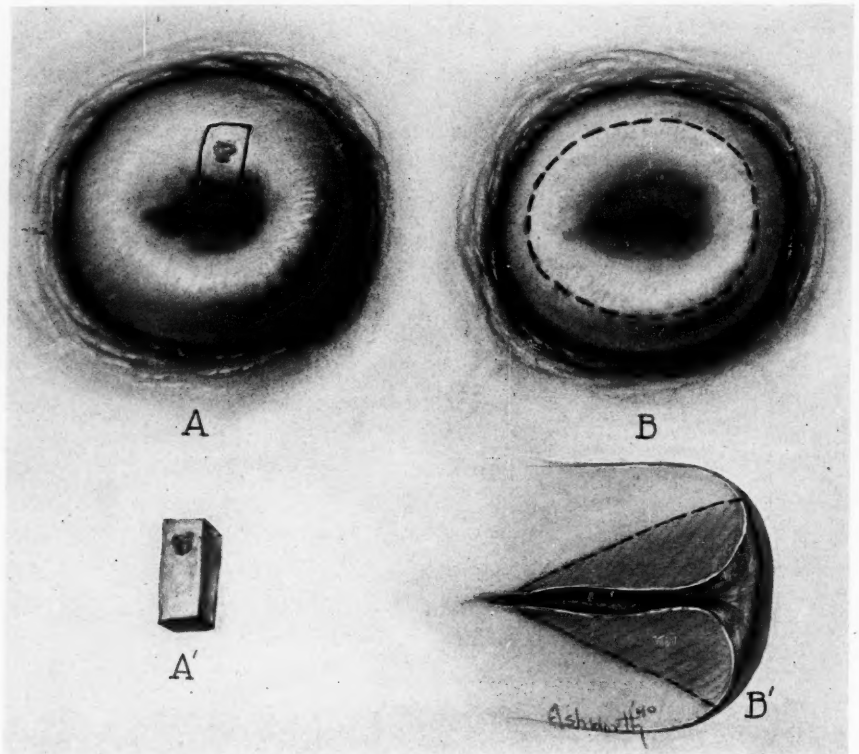

Fig. 6. Schematic representation of the method of obtaining material for histologic study. A represents a suspicious area on the anterior lip of the cervix uteri, with the dark lines indicating the direction of incisions for removal. A′, the shape of the excised block of tissue. B, a larger suspicious area, which in some cases may advantageously be removed by a cone-shaped enucleation of the endocervix, together with a portion of the portio, as indicated by the circularly dotted line and also as represented by shaded area in B′.

It is important if a conical enucleation of the endocervix is done, that the dissection be carried sufficiently proximally and widely so that all the mucosa is obtained. (Fig. 9B.) This is not a simple office procedure and should not be done with the small endothermy units common to

office practice, although such a procedure is advocated by some.

The importance of this cannot be overstressed in these instances where varying portions of the mucosa of the canal have undergone stratification (squamous cell metaplasia) and the glands are filled with stratified epithelium. This in the absence of any further change is occasionally erroneously diagnosed as cancer. However, when this stratified epithelium really takes on the appearance of cancer, it becomes of vast practical importance to know whether it is an invasive tumor, even though minute, or merely an area of non-invasive carcinomatoid change, and, if the latter, whether it has been entirely removed. This requires the preparation and study of numerous microsections—which cannot be done in a few minutes while the patient is on the operating table under anesthesia.

The clinician must therefore do his part by properly obtaining tissue. It then becomes the problem of the pathologist, if the clinician is not versed in gynecologic pathology, to make a histologic diagnosis. This ordinarily provides the key to the problem of the patient's subsequent management. However, where the lesion is one that presents difficulty in diagnosis, and this does happen, it is desirable that the clinician have sufficient understanding and experience to appreciate the pathologist's dilemma. Thus the patient's interests may be protected and her welfare not jeopardized by the use of therapeutic measures for which there is strong emotional impetus but a poor factual basis.

The diagnostic problems presented by these areas of non-invasive carcinomatoid change (precancerous lesions) have been well described by Novak,[21] Freedman,[22] Schiller,[23] Te Linde,[24] von Franqué,[25] Pemberton and Smith,[26] and more recently by Stevenson and Scipiades[27] and others. It is obvious that they offer problems toward which various students of the question assume varying points of view. With this as a basis, the therapeutic approach varies from one of careful study and simple removal of all suspected tissue, if the original operation for the removal of tissue for biopsy has not accomplished this, to a thoroughly energetic program of radiation, radical operation or radiation and operation. In other words, we find illustrated here the conservative versus the radical therapeutic approach to a problem whose true significance is probably little better understood now than it was by Virchow[28] eighty years ago.

Our attitude toward these borderline lesions of non-invasive carcinomatoid change when sufficient tissue is available for adequate study has been similar to that of TeLinde, Novak, and a few others, one of conservatism. Our limited experience is borne out by the studies of others,[24,27] where following removal of such suspicious cancer-like lesions, nothing more was done. Especially valuable are the observations of Stevenson and Scipiades on eighteen patients so afflicted. The diagnosis of "non-invasive potential carcinoma" had been made in thirteen of these, from three to seventeen years before. The outcome is known in eleven. Only one was treated with radium and two were under observation for less than six years. Two of these eleven patients later developed cancer, one nine years after she was first seen when she had a full-blown cancer of the portio, the other three years after her biopsy when she died of pernicious anemia and the cervix removed at autopsy revealed a small bona fide cancer detectable only on histologic study. The others remained well.

It is obvious that some of these borderline lesions that are coming to our attention more frequently, now that early malignant changes are being more carefully sought, offer special problems for the clinician and the pathologist. The present status of our knowledge based on adequate study of tissue and follow-up of patients is still not sufficient to warrant a hard and fast attitude on the subject. This certainly is not conducive to a complacent state of mind. As a consequence, it has led some to adopt the attitude that granted the le-

sion of non-invasive carcinomatoid change is not definitely cancer, nevertheless, if it is treated as such there is eliminated the danger of future malignancy.

This is often regarded as a straightforward, practical, point of view which presumably leaves little room for improvement. It is, however, an attitude based largely on fear and lack of information. This not only stifles inquiry and progress, but leaves in its wake women too often in the prime of life who have become victims of well intentioned but ill conceived radical therapy. Further study of such surgically removed organs often reveals little to justify such procedure.

CONCLUSIONS

The conclusion is permissible that the problem of early and especially of covert cancer of the cervix uteri and the allied pathologic problem of non-invasive carcinomatoid change often require special consideration and study. It therefore follows that adequate removal of tissue from a so-called suspicious area together with a careful and competent histologic study are the foundations on which rest the diagnosis of early cancer of the cervix uteri.

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THE PRESENT STATUS OF RADIUM TREATMENT OF CARCINOMA OF THE UTERINE CERVIX

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IT seems rather remarkable that, after more than fifty years of intensive study of cancer of the uterine cervix, the medical world knows so little about the laws that govern its origin and growth. It seems equally remarkable that so many important observations about this cancer appear to have been forgotten, probably because they were made when surgery alone offered any hope of cure and before any one was conscious of the therapeutic value of radium. The modern cancer student now usually has a background of some animal experimentation, a study of physics, and has had an intensive training in therapy with radium and with the heavy voltage Roentgen ray. Yet he rarely has had much of an apprenticeship in cancer surgery, and in all probability was taught erroneously that the radical operations for cervical cancers were only conspicuous failures attended with an operative mortality of 20 per cent. Usually he is not much interested in what happened in the surgical era.

Yet nearly all that we know of the methods of growth and extension of untreated cancer was learned during the surgical period. When men were attempting to cure extensive cancers they had remarkable opportunity to see all types of invasions. Among the many things that they learned we note the following:

Cancer may not grow at the same rate of speed in women even in the same age group and same body build.

Cancer may use different pathways for extension and finally present such great variation in its morphologic picture that one might almost conclude that they were different cancers. Ries and other early workers described a number of these, many of which now constitute the subgroups in the recent League of Nations classification.

The average duration of untreated cancer is about two years; the extremes are shown in Table 1. The reasons for these variations have never been determined. There was some evidence that cancer grows more rapidly in the anemic flabby body than in the compact well nourished individual, yet there are many exceptions to the rule.

TABLE 1

DURATION OF LIFE IN UNTREATED CANCER

Stage 4 Cancers (Schmitz)

Symptoms before Treatment	Cases	Survival after Treatment, Months
0–3 months	13	7
3–6 months	17	7½
6–9 months	13	9
9–12 months	8	7
12–18 months	14	12
18–2 years	3	8½
2 years and over	14	10½
Unknown	2	14
Total	84	

It was well recognized that there was great variation in the time when the glands became involved. Usually, but not always, the parametrium seemed to be first invaded. Yet enlarged firm glands have been found to be free from cancer, and enlarged only from absorption from the inflammation of cancerous ulcer. On the contrary, small normal-appearing glands have shown definite cancerous infiltration even with a soft parametrium, and in quite recent time Bonney showed that the obturator glands were invaded very early—a fact that had not been recorded by the earlier observers.

George Winter noted that patients whose cancers presented everting or papillary or cauliflower forms usually survived longer than those who came with cancers inverting and infiltrating.

Schottlaender, as early as 1906, attempted to link rapidity of growth with the histologic cell picture, giving the foundation on which Broders and Martzloff laid their work many years after.

With such a kaleidoscopic mass of facts before us, no one should be surprised to learn that a definite percentage of patients who seemed to be inoperable before operation survived the radical removal and the five year observation period without evidence of recurrence, and that some patients whose visible growth was limited clearly to the cervix, died from recurrence in a few years after a radical operation. There is no doubt but workers in the surgical era proved that there were great variations in the malignancy of what appeared as the same type of cervical cancer.

Radium when first introduced was given only to inoperable cases, but such remarkable results attended its use that many felt that they were justified in radiating early operable cancers instead of operating upon them. In spite of the fact that no one knew anything much about proper doses, foul smelling ulcers cleared up, hemorrhage was arrested, patients gained in weight and strength, and some who even looked as if they were about to die seemed tremendously improved.

The few fistulas which followed the treatments seemed nothing in comparison to those attending surgery. More than that, patients left the hospital on their own feet, and cancer wards no longer were filled with dying women surgery had failed to cure. It is no wonder that the world fairly went mad about radium. I much doubt if any other discovery in recent medicine has been as dramatic.

Time has proved that radium cannot accomplish all that was once claimed for it. It has done wonders, but probably the limits of its therapeutic possibilities have been reached; there is no doubt whatever that the combination of deep Roentgen ray and radium accomplishes far more than either treatment used alone. No one, however, feels that even this combination therapy is the final answer to the problem of successful treatment of cancer of the uterine cervix.

The reason for this change of thought about radium has followed the observations that the element is unable to kill cancer more than a few centimeters from the point of application, unless tremendous dosage is given with the bomb. Even then there may be cancer cells that do not succumb to the rays, in the tissues which should be perfectly rayed. Unfortunately no one knows much about these radium-resistant cancer cells.

When radium first came into therapy, it was thought that a capsule placed in the cervix, which is practically the center of the pelvis, would completely ray all cells within the pelvic walls, killing all the cancer cells within the pelvis but not harming the normal tissues. There seemed much clinical evidence for such belief; not only did the local lesion shrink up and disappear but occasionally the treatment seemed to cure cancers with parametria so involved that they had to be classed as inoperable.

Few have removed such uteri to study the pathologic picture. Following our gland resection operations it has been necessary occasionally to remove the pelvic organs in such cases. In some we have not been able to demonstrate cancer cells in the parametrium, forcing the conclusion that the infiltration had been inflammatory only from absorption from the infected ulcer, which cleared up when the ulcer had been cured; this of course means that the case had not been inoperable. When unchanged cancer cells were found in the parametrium and the glands were found not involved, many questions naturally arose. For instance, one would wonder whether this cancer was of comparatively low malignancy and was invading slowly, and whether it would have lain dormant for some

time after the inflammatory products had cleared up after radiation if it had been radiated only and not operated upon. Cases like these with limited invasion must have been the bulk of inoperable cases which became five year cures after radical operation in the older days, in the surgical era.

We now know that all that we hope radium will do, when inserted into the lower uterine canal and cervix and the dose is adequate, is to take care of the cancer in the lower uterine and cervical walls. It cannot kill cancer cells even in the parametrial cervical-uterine margins; those must be taken care of by cross-firing from the vagina, by parametrial needles as in George Ward's plan, or by deep Roentgen ray.

Yet we also have learned that practically the radiation never comes up to the possibilities which physics shows us it has. This I have well proved in a study of my own series. The untrained technician pays little attention to the meaning of screening or proper distance, but just puts the radium in anyhow and hopes for the best. Naturally he is at his worst when the surfaces to be radiated are irregular, as in large deep sloughs with a bore and depth of a couple of centimeters, or when the cancer is extending irregularly down the vaginal well. Then the instruments devised to hold the radium in the infiltrated fornix fail to keep it in the place where it is expected to be. Very often indeed will the careful technician find that he has radiated all the wrong places, and be reminded of Sampson's bizarre films showing radium in the cavity of the uterus far distant from the side wall where it was intended to be. I have no doubt the method of radiation adopted is not nearly as important as the detail with which it is carried out; the cure rates from well conducted clinics using different methods of radiation are essentially the same. The beginner will find it helpful at first to *x*-ray each case after placing the radium and packing it in place, in order to learn how much it has slipped or fallen away from the position in which he intended it to be.

Nearly all radiologists at present employ the fractional dose method, repeating treatments not only successively to radiate all points desired but also to ray the greatest possible number of cells at the time they are dividing. Whether the treatments are daily or weekly depends upon what technique is followed. The filtration and the distance between the desired point of radiation and the capsule is usually the same in all treatments.

The combination of Roentgen ray and radium will improve results; when technical difficulties have made it impossible to apply radium in an ideal manner, and the capsule is not just where it should be, a broad beam of deep Roentgen ray may be a life saving measure. My own results prove that this is true. With a combination of radium and deep Roentgen ray the five year cure rate in eighty-two cases was 39.7 per cent, nearly double the number obtained from radium alone in a series approximately equal in size, treated just before we began to use Roentgen ray as part of the combination treatment. Neither series included any case that had been operated upon radically or even had had gland resections. The detailed report will soon be presented by Morton. (I operate radically and after preliminary radium treatment, in all the very good surgical risk cases where there are very early cancers.) The series just noted unfortunately is small. Were it very much larger, I much doubt if the history, other records and the follow-up could be nearly so good. My total cervical cancer series is only 750 cases, but the follow-up is complete on each case from time of treatment to date for twenty-four years. Nearly everything, height, weight, body measurements, all kinds of blood studies, basal metabolism, detailed family history, dietary history, and, in some cases, hormone studies have been made. Blood transfusions are routine.

The dosage of *x*-ray has changed very much during the course of the series, while

the *x*-ray men were trying to find the optimum dose, just as we had to do with radium. Our *x*-ray therapy is under the direction of Dr. Robert S. Stone, head of the *x*-ray department, who fortunately is also much interested in cancer therapy. The radium is given by members of my own staff.

In this last series, we used the Memorial Hospital technique for radium; most of the cases were treated with a 200 K.V. constant potential General Electric X-P tube, a few with our Sloan high-frequency generator operating at from 1000 to 1200 K.V. In general the pelvis was rayed through two 10 × 20 cm. fields anterior and posterior. The number of Roentgens varied tremendously; in the very beginning a few cases had only 1000 per field, then quite a number had from 1600 to 2200 per field, and in the latter part of the series more than 3000 were given for each field. What neutron therapy will accomplish remains to be seen.

The time when the Roentgen ray treatment should be given has occasioned some debate. All the men in my group feel that it is optimum before radium and that the course should be completed before the radium treatments are begun. To my mind there is always a chance of causing metastases when dilating or otherwise manipulating a carcinomatous cervix that has not had Roentgen ray treatment previously or at least one treatment with radium placques placed in the vagina against the cervix before dilatation.

When Stone began using the big 1200 K.V. machine and was trying to find proper dose levels, quite naturally many patients were made quite sick, sometimes so sick that we had to change our sequence and give radium before the Roentgen ray in order to get it into the treatment at all. Now, however, extremely sick patients are not common and the Roentgen ray is given first. It seems to me that fewer pelvic inflammations develop and become major complications when the Roentgen ray is so given. When such conditions develop they may be extremely troublesome, disrupt or cause postponement of the treatments or keep the patient in bed for many weeks. That they do occur is everywhere evidenced in the literature.

In 1936 not only did Bowing and Fricke report major complications in 5.6 per cent of 495 cases, but Reiles and Fobe had peritonitis follow radium in six of their 100 cases.

The question of radium-resistant cells is most important and unfortunately is far from settled in spite of a tremendous and very confusing literature. That there are such cells is a fact—cells which have lived through tremendous doses of radium and of deep Roentgen ray and which are found at operation or autopsy. Some cancers which seem to be resistant to radium disappear under Roentgen ray. I wonder, therefore, whether these cells are actually resistant to radium or whether the real trouble is not a faulty radium treatment. I now consider a cell resistant only if it persists three months after the combined treatment of radium and Roentgen ray, and then only if it is situated in a part of the uterus where it could have been acted upon properly by both of these therapeutic agents. Most such cancers in my series have had transitional cells (Martzloff's classification) predominating, but most of the cancers in the entire series also have transitional cells predominating. Usually, however, the persistent cell in the tissue depths is more differentiated than that in the biopsy specimen from the surface of the cervix.

I have no way of calculating how frequently we find these cells, because the series is small and the technique is constantly changing. They were common findings in my earlier operations even though the cancers had received what then was called adequate radiation. We find them less commonly now, yet we occasionally find them (as we have said before) in spite of more than 5000 mc. hours (Memorial technique) and more than 3000 Roentgens from the 1000 K.V. tube to each of two

anterior and posterior fields each 10 × 15 cm. given by a very competent technician who is also a physician. Within the next few months, I expect to make a detailed report of my findings.

Neither I nor my co-workers, Schulze and Morton, have ever been able to confirm from study of my cases the theories that the histologic cell type of the cell was a major factor in curability of the patient. Unfortunately the material is so small, as is that of nearly any other series available for study, that by the time the tumors are broken down into the same cell types and the same clinical grouping, i.e., the same estimated amount of anatomic invasion—using Schmitz's classification—the resultant subdivisions are too small to stand up under the mathematician's computations. There remain also other factors, such as the blood supply of the tumors, the type of vessels, their location, the type and condition and type of the patient, etc., points suggested by Norris, all of which defy evaluation.

And while not actually germane to this subject, the report of Cathie in February, 1939 is very interesting. This author attempted to ascertain in Manchester the possible relationship between the histologic grading of primary tumors and their metastases in a series of sixty-seven cases in which adequate biopsy material was available from the primary lesion and from dissections of tumor-bearing lymph nodes which drained the region. The cancers were from the mouth and genitalia and were correlated with their metastases in the regional lymph nodes of the neck and groin.

In thirty-four cases the grading of both primary and secondary growths was the same. In thirty-one cases the metastasis was more differentiated than the primary growth. In two cases it was less differentiated.

The question whether operation should be performed upon patients who are excellent surgical risks and whose cancers are small and definitely limited to the cervix is less important now, when radiation has improved and is combined with intensive Roentgen ray therapy than it was when the most extravagant and absurd claims were made for the therapeutic action of radium. At that time my cure rate with radical operation after radium was twice what I obtained after radium alone in stage I and II (Schmitz) control cases. I am continuing the study chiefly to learn just what the combined therapy is accomplishing. I will abandon it when I find there are no radium-resistant cells in early cases which have been adequately irradiated and when the cure rate with the combined treatment equal that of my surgery.

Unfortunately the cancer student grows old equally fast with his patient and each change in radiation technique means another five years wait before one can tell what his change of technique has accomplished. The radiologist, when radium treatment was new, seemed to think that only the physicist was important, forgetting the pathologist and the fact that the changes they found in surface tissues might not be present in the deeper structures of the tumor.

Radical operation, however, is justifiable only when it can be done with little or no mortality and without any fistulas or other disagreeable major morbidity. In contrasting postoperative convalescence with the stormy period that now follows adequate Roentgen ray therapy, which is paramount to telling the woman she has a cancer, I am not certain which is the lesser of the two evils. Under no circumstances may the surgeon think that an ordinary panhysterectomy is, ever was, or ever can be a radical operation.

CONCLUSIONS

1. Present day cancer students may review with profit many of the fundamental investigations that were made by their predecessors long before the advent of radium into cancer therapy.

2. Radium never can be regarded as a "cure-all" for cancer of the cervix.

3. While there remains too much difference between the theoretical possibilities of radium treatment and what it actually accomplishes in cancer of the uterine cervix, it is not likely that the present day methods of application will be greatly improved.

4. The results obtained in leading clinics with radium therapy are essentially the same.

5. The combination of deep Roentgen ray and radium therapy gives a larger five-year cure rate than either treatment used alone.

6. Cancer students when reporting cures must not forget that some untreated cancers of the uterine cervix may allow the patient to live for years.

7. No definite relationship between curability, radium resistant cells and the histologic cell type of the primary tumor can be established in my series.

8. The ordinary panhysterectomy, with removal of the tubes and ovaries, is not a radical operation even for very early cervical cancers.

GRAVES holds it [cancer of the cervix] to have a life history of many years; the initial stage, of chronic cervicitis, being a long one, and the second, shorter, stage being marked by an actual cancerous change, a piling up of cancer-like cells which have not yet become invasive. Perhaps such lesions have not usually been recognized by pathologists, but it is more likely that surgeons have been content to repair rather than amputate the chronically inflamed and lacerated cervix.

From—"A Textbook of Surgery" by John Homans (Thomas).

TOTAL VERSUS SUPRAVAGINAL HYSTERECTOMY

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OPERATIONS on the uterus for benign conditions constitute a large percentage of the major operative procedures on any gynecologic service. The type of operation to be performed in any given case depends not only on the pathologic condition, the patient's age, her marital state, the state of her general health and to some extent her wishes in the matter, but also on the experience of the surgeon and the results he has obtained with various types of operations in similar cases. In some cases more or less satisfactory results will be obtained with a variety of different operative procedures, but following some of these there may be the probability of future trouble which will require a second operation or frequent treatments. In my experience, in many cases in which trouble follows operation a cancer phobia develops to a greater or lesser degree. Many of them do not return to the original surgeon because they think he does not understand their case.

One of the most controversial points among gynecologists is whether to do a total abdominal hysterectomy or a supravaginal amputation in the majority of cases in which it is advisable to remove at least part of the uterine body. In all discussions on this subject it is freely admitted, even by ardent supporters of the more radical procedure, that statistics from the country as a whole will show a definitely higher mortality and morbidity when this operation is performed. This does not mean, however, that the operation is at fault, but simply that it is being attempted by some surgeons who are not familiar with the various steps of a difficult operation. I am satisfied that when total abdominal hysterectomy is done by competent surgeons in a large series of cases, the end results are better, the morbidity is less and the mortality no greater than when a subtotal abdominal hysterectomy is done in a similar series of cases by the same experienced surgeons. For the occasional operator or for any surgeon who has not taken special pains to become thoroughly familar with the technique of a total abdominal hysterectomy, my advice would be to continue doing the subtotal operation in a large majority of his cases even at the risk of leaving an infected cervix, which might require treatment or removal at a later date. A neglected infected cervix is a definite predisposing cause to complications; the most frequent of these is thrombophlebitis and the gravest are pulmonary emboli or the later development of cancer.

I do not agree with those who say that the only advantage of total abdominal hysterectomy over subtotal operation is the protection against the later development of cancer. If this were the case, I would not feel justified in advising the total operation as often as I do. Just what added danger there is of malignant disease developing in a cervical stump over the normal incidence of cancer of the cervix in a like number of cases is hard to determine. It is known, however, that cervicitis is a very common sequela to subtotal abdominal hysterectomy and that chronic irritation from infection is a definite predisposing cause of cancer. Statistics are very unreliable in such cases and vary a great deal in different countries and among different surgeons in any one country. The weight of statistical evidence, however, is that cancer occurs in probably not more than 1 or 2 per cent of cases in which a subtotal hysterectomy has been performed for benign conditions. Henriksen, in 940

cases of carcinoma of the cervix observed at the Johns Hopkins Hospital, found that carcinoma developed in the cervical stump in 2.3 per cent of them. At The Mayo Clinic, from July 1, 1930 to December 31, 1938, inclusive there were 1,489 cases in which a pathologic diagnosis of carcinoma of the cervix was made and of this number, sixty-five or 4.4 per cent were cases of carcinoma of the cervical stump. There is no doubt that this condition is reported much more frequently at the present time than it was formerly.

Von Graff reported on nearly 1200 cases in which cancer developed in the cervical stump and there is no doubt that many such cases are never reported. In most of the cases, as shown by C. H. Mayo and C. W. Mayo, the condition is not diagnosed until late and until the outlook for cure is not good. In a series of sixty-five patients who were treated for carcinoma of the cervical stump at the clinic and whom we were able to trace, we found that only thirteen, or 20 per cent, had lived five years. From January 1, 1910 to December 31, 1938, inclusive, we have seen 164 cases of carcinoma of the cervical stump. In twenty-four of these cases subtotal abdominal hysterectomy was performed at the clinic and in 140 cases it had previously been performed elsewhere. In 136 of these 164 cases, the malignant condition was recognized for the first time at least one year after the abdominal operation had been performed, and this interval, I think, should be accepted as evidence that the malignant lesion did not exist at the time of the supravaginal operation. Besides the cases of cervical cancer, we have seen many cases (more than 500) in which cervicitis with leucorrhea was sufficient to require treatment. In many of these cases there was no history of the occurrence of leucorrhea before the body of the uterus had been removed. Furthermore, recent investigation has shown definitely that cervicitis is frequently a focus for infectious arthritis, myositis, iritis and other disabling diseases. In addition to the danger of cancer and cervicitis, one must recognize the danger of benign tumors, such as fibroids and cervical polyps, developing in a retained cervix. At the clinic we have operated on three patients for fibroids in retained cervices and on many who had polyps.

The objections raised to the total operation, such as shortening of the vagina and a greater tendency toward prolapse of the vaginal vault, do not hold if the cervix is enucleated out of the vaginal vault and the latter is properly secured to the tissues from the base of the broad ligaments, uterosacral ligaments and round ligaments and if any relaxation or lacerations of the lower pelvic diaphragm are cared for at the same time or soon afterward. There is no doubt that obstetricians today are aware of the importance of puerperal gynecology, but Richardson has stated that "Recent reports from some of our best obstetric clinics reveal that late follow-up examinations disclose unsatisfactory conditions of the cervix and lower birth canal in 50 to 75 per cent of women who have borne one child or more." The contention that the total operation is a frequent cause of dyspareunia is unfounded. When this is a postoperative complaint, it is generally due to fixation of the ovaries to the vault of the vagina and to diminished vaginal secretion; this latter condition can be overcome by the use of a nonirritating lubricating jelly.

In reviewing the literature, it is interesting to find how infrequently physicians who have large gynecologic practices report cases in which complications or sequelae which require treatment occur after subtotal abdominal hysterectomy, whereas other physicians report seeing such cases frequently. It is not surprising that the former do not encounter cases of arthritis, neuralgia and iritis, but one would expect them to encounter an occasional case in which local disease had developed in the cervix itself. This can be accounted for, in part, by the fact that the patient fears that the operation was not

satisfactory and she therefore goes elsewhere for advice. The fact that subtotal hysterectomy had been performed elsewhere in 140 of the 164 cases of cancer of the cervical stump which we have seen at the clinic, lends strength to this argument.

Morbidity is frequently due to pelvic peritonitis of low grade, which these patients fortunately stand well, to thrombophlebitis and to adherent loops of small intestine in the pelvis. I have always thought that when a total hysterectomy is performed after surgical preparation of the vagina there is less chance of infection than there is when the subtotal operation is performed and the cervical glands are cut across and frequently are traversed with sutures. In many cases infection is already present. When the cervix is coned or is destroyed by cauterization, added protection from infection is not given as these procedures leave a sloughing region continuous with the operative field and peritoneum. Furthermore, such procedures do not protect against the occurrence of epithelioma of the cervix because this neoplasm starts on the portio vaginalis rather than in the cervical canal in most cases.

No matter which operation is performed, I am satisfied that a very important protection against subsequent trouble, not only while the patient is in the hospital but also for months or years afterward, is the care taken to prevent loops of small intestine from becoming adherent in the pelvis. This condition is the result of a pelvic infection of low grade, which is frequently caused by the use of drainage or occurs because all raw surfaces were not covered properly with peritoneum. If it is not possible to cover these raw surfaces in the ordinary way, it is advisable to utilize the sigmoid or appendices epiploicae. I have seen several instances of subacute intestinal obstruction months after a patient has left a hospital after what was regarded as a normal postoperative course and I have seen one case of complete obstruction fifteen years after a pelvic operation in which a loop of small bowel apparently had been adherent deep in the pelvis all that time. I am satisfied that many patients who die of peritonitis could be saved by early recognition of intestinal obstruction and freeing of a loop of small bowel adherent in the pelvis before infection spreads from the lumen of the bowel to the free peritoneal cavity.

In many cases of uterine fibroids in which the mass is not larger than a three months' pregnant uterus and in which the only symptom is menorrhagia, the advisability of performing a hysterectomy or treating by irradiation has to be considered. There is no doubt that there is legitimate ground for a difference of opinion if a subtotal hysterectomy is considered sufficient, but if there is any pathologic lesion in the cervix, I believe the best interests of the patient are served by removing the uterus completely. Radium and Roentgen therapy give excellent results with little inconvenience and hospital expense to the patient and practically no mortality. Burnam reported treatment by radium in 1800 cases without a death. One cannot, however, compare these statistics with surgical statistics because the former represent treatment in a very select group of cases. In all complicated cases, necessarily, treatment is by operation and many of the patients are exceedingly bad risks in whom operations are difficult. Moreover, in an occasional case in which the result is listed as good following treatment by radium months or even years before, subsequent treatment is required for leucorrhea, menorrhagia, adnexal trouble or malignancy. At least once a year I see a case in which carcinoma of the body of the uterus has occurred after the use of radium therapy. Statistics show that in an unselected group of cases in which operation is advisable and is performed by a member of the visiting staff of most accredited hospitals the mortality rate associated with subtotal abdominal hysterectomy is about 4 per cent and that asso-

ciated with total abdominal hysterectomy is about 6 per cent.

There are reports of cases in which cancer developed in the vault of the vagina after a total abdominal hysterectomy, but I never have heard of such a case in which carcinoma of the vault of the vagina followed a vaginal hysterectomy. It would be impossible to prove but I have seen so many cases in which a total abdominal hysterectomy was supposed to have been done and in which some cervical tissue was left that I believe that such cases should be listed as cases in which carcinoma developed in the cervical stump rather than as cases in which the growth was vaginal in origin.

From January 1, 1934 to December 31, 1938, inclusive, hysterectomy was performed for benign conditions in 3,149 cases at the clinic. In the 1,776 cases in which total abdominal hysterectomy was performed, twenty-two or 1.2 per cent of the patients died; in the 766 cases in which subtotal abdominal hysterectomy was performed, seven or 0.9 per cent of the patients died, and in the 607 cases in which vaginal hysterectomy was performed, nine or 1.5 per cent of the patients died. During the years 1936, 1937, and 1938, I performed 784 hysterectomies with six deaths, or a mortality of 0.76 per cent; 196 of these were vaginal hysterectomies with one death, a mortality of 0.51 per cent.

In recent years I have become more and more convinced that a total hysterectomy is advisable in most cases in which it is necessary to remove any of the uterine body of women who have been delivered of children by the vagina and who are close to or at the menopausal age, provided the surgeon is familiar with the technique of such an operation and can complete it within an hour. I am satisfied that the three most important considerations in a low operative mortality are: (1) a well given anesthetic; (2) adequate exposure; and (3) no unnecessary delay in completing an operation. Few abdominal operations should keep a patient on the operating table more than one and a half hours.

There is no doubt that spinal anesthesia, as given today by specialists in this field of therapy, is a relatively safe procedure, but I do not feel that it is as safe as a well given inhalation anesthetic by an expert with a modern anesthetic machine and the various gases that are now used under direct control. If I did not have an excellent anesthetist, I certainly would use spinal anesthesia much more often than I do. I am satisfied that spinal anesthesia always makes an operation easier for the surgeon but a little more dangerous for the patient.

In any consideration of hysterectomy it is also necessary to consider the disposition of the adnexa. Some surgeons feel that if the uterus is to be removed there is little to be gained by saving the tubes and ovaries, whereas others feel that the ovaries should be saved whenever possible. If the patient is close to or past the menopausal age, there can be little difference of opinion. Most surgeons agree that cutting the infundibuliform ligament close to the brim of the pelvis and total removal of tube and ovary on both sides are indicated if the uterus also is to be removed. The Fallopian tubes are of no use if the uterus is removed, but the ovaries are of definite value to the patient still in the child-bearing period of life. My practice has always been to save normal ovarian tissue when possible in young patients when operating for benign conditions. I would sooner consider the possibility of a second operation for some ovarian condition than to remove both ovaries of a woman less than 40 years of age. In recent years I have adopted the practice of removing the Fallopian tubes whenever I have to do a hysterectomy. I never could see any advantage in leaving them and I frequently have on my service patients in whom a second operation is made necessary on account of tubes that have been left following a hysterectomy. If care is taken in their removal there should be no interference with adequate blood supply to the ovary. The tubes develop

along with the uterus from the Müllerian ducts and their principal blood supply comes from the terminal branches of the uterine arteries. When these vessels are cut the ovarian vessels have to supply the tubes as well as the ovaries. They are able to do this all right but with the slowing of circulation clotting often takes place in the venous plexus in the mesosalpinx and this may well be the starting point of a pelvic thrombophlebitis. On my own service I certainly have had less trouble with pulmonary embolism and other less serious complications since I have been doing the more radical operation. As far as I can tell, the ovaries function normally in just as high a percentage of cases.

Most authors who advise the more frequent use of subtotal hysterectomy have figures to show that the bladder, ureters and bowel are less frequently injured when the less radical operation is performed. The only reason I can see for this is that some surgeons who are doing total abdominal hysterectomy do not see accurately what they catch with each forceps or include with each stitch. In the technique that I use, I ligate the uterine vessels at the same point in all cases of benign lesions no matter whether I do a total or a subtotal hysterectomy. The only difference is that I have to tie separately an extra branch that goes to the cervix on each side in all cases in which I perform a total hysterectomy. Abnormally situated ureters are occasionally noted, but as a rule they run a normal course unless pressed upon by uterine or ovarian tumors. The way to avoid them is to keep close to the uterus. In all cases of doubt it pays to isolate them before attempting to control deep pelvic bleeding, and in peritonealizing the raw surface all stitches should be superficial.

Injuries to the bladder are probably most often due to stripping the bladder from the cervix by blunt or gauze dissection rather than by sharp dissection. This is especially true in cases in which the uterine lesion is complicated by pericervicitis. Personally, I prefer a sharp knife to scissors for this part of the operation.

TECHNIQUE

The especially long instruments and the Mayo fibroid hook which I use for performing hysterectomy are shown in Figure 1. A Kocher hemostat is first placed close to the right side of the uterus; it includes the proximal parts of the right round ligament, the right Fallopian tube, the right utero-ovarian ligament and the upper part of the right broad ligament. Another hemostat is placed on the right round ligament just distal to the first forceps; the round ligament is cut between them and the peritoneum is cut on each side of the round ligament for a distance of 1½ or 2 inches (3.8 or 5 cm.). (Fig. 2.) The fimbriated end of the right Fallopian tube is now grasped with forceps and the tube and ovary are thoroughly inspected. If it is decided to save the ovary but remove the tube, I catch the vessels close to the tube with one or two clamps and then cut the ovary free from the uterus by cutting the utero-ovarian ligaments between clamps. I like at this time to tie securely the end of the round ligament, the utero-ovarian ligament and the various vessels secured by forceps after removal of the tube. The various steps of the operation as described are now repeated on the left side of the uterus, but in most cases the ovary is also removed on the left side as it is less liable to cause postoperative discomfort, but if the left ovary is the better of the two, it is saved and the one on the right side is removed. Traction is now made on the forceps placed on each side of the uterus. The peritoneum is cut in front and the bladder is freed from the cervix and vault of vagina by sharp dissection. (Fig. 3.) As a rule, it is necessary to ligate one small artery in the vesico-cervical fold on each side. By continuing traction on the uterus and drawing it down over the symphysis pubis, the uterosacral ligaments are exposed. These ligaments are then cut from the posterior surface of the cervix. At this time, I also like to cut the

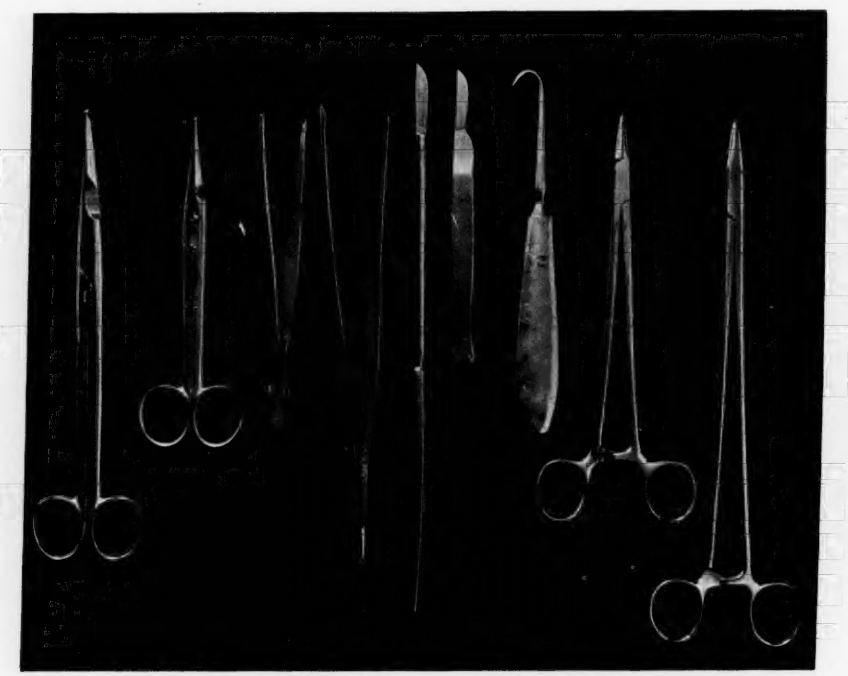

Fig. 1. The Mayo fibroid hook and long-handled instruments are a definite help in most cases.

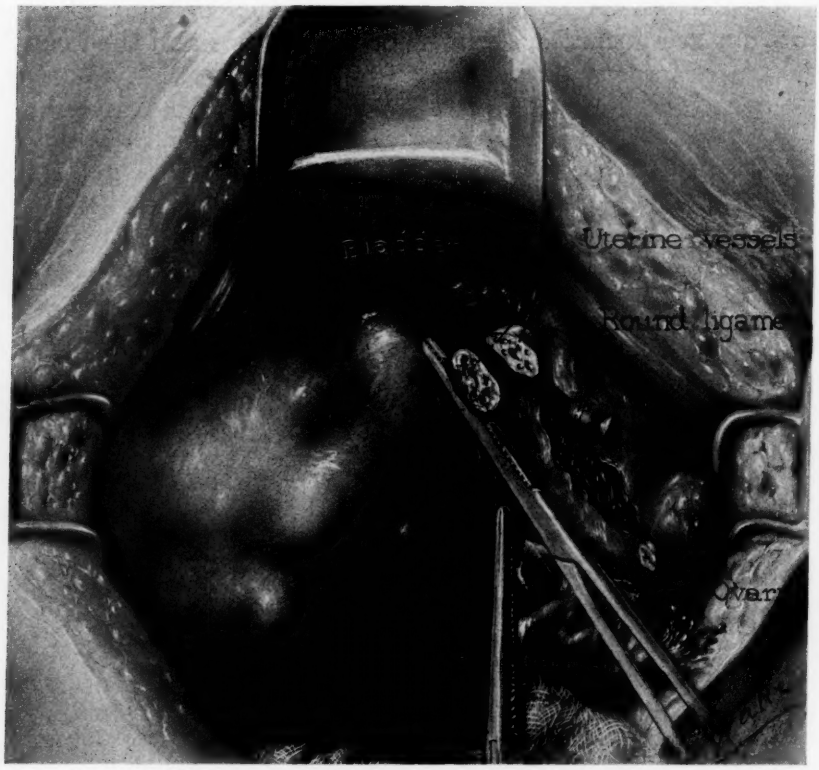

Fig. 2. Cutting through broad ligament; stumps of uterine vessels round ligament and utero-ovarian ligaments have been ligated.

peritoneum across the posterior surface of the broad ligament.

The uterine vessels and the cardinal ligament in the base of the broad ligament are now caught at about the level of the internal os with three Kocher hemostats that are applied almost at a right angle to the cervix, and the tissues are cut between the upper and middle forceps. If this technique is followed, I do not believe it is necessary to isolate the ureters as there is no chance of injuring them if the forceps catch right up to the cervical tissue. It is only in the exceptional case in which some bleeding occurs deep in the base of the broad ligament or along the side of the vagina that I feel that it is necessary to locate the ureters before controlling the bleeding. I do not believe that inserting ureteral catheters before starting the operation is a necessary or good practice. The point at which the uterine vessels are secured is the same whether one is doing a total or subtotal operation. The only difference is that if a subtotal operation is contemplated the cervix is cut across at the level at which the uterine vessels are clamped and the cervical canal is closed by two or three stitches, whereas when a total hysterectomy is contemplated the pericervical tissues are cut and the cervix is enucleated from the vaginal vault. If the surgeon works close to the cervix in this part of the dissection there is no danger of injury to ureter, bladder or rectum. Constant traction on the uterus by means of Mayo hooks and the use of a knife with a long handle or a long pair of scissors make this part of the operation easy. (Fig. 4.)

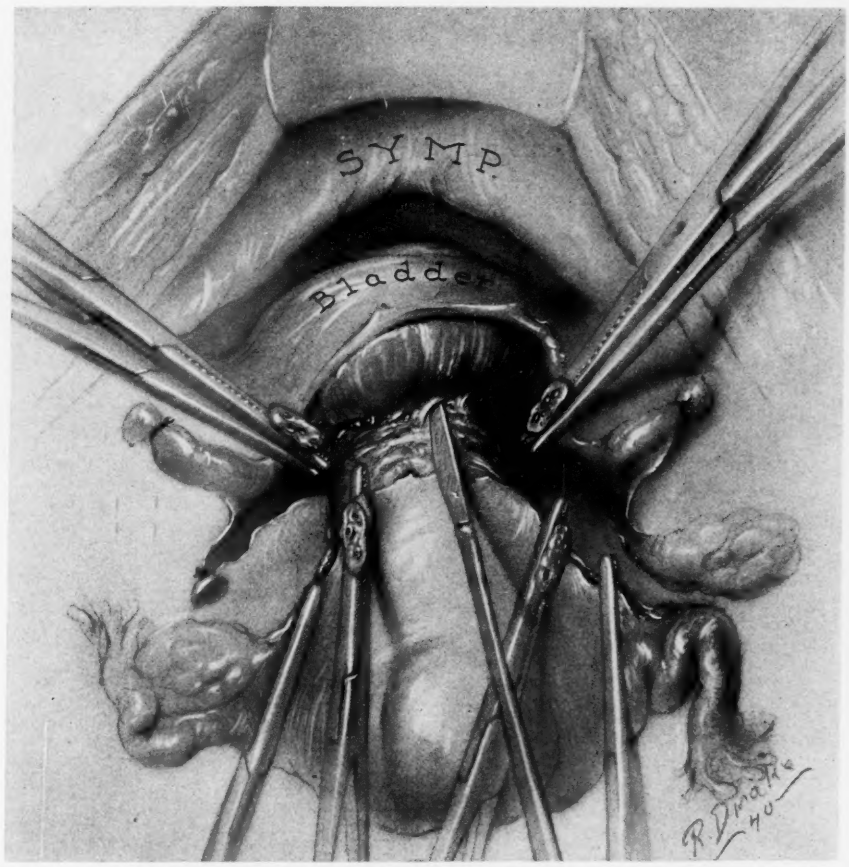

Fig. 3. Separating bladder from cervix by sharp dissection; uterine vesselsdoubly clamped at right angles to cervix.

As soon as the vagina is opened I insert a strip of gauze about 2 inches wide and 12 inches long, which has been dipped in tincture of merthiolate. This is left in place until the third or fourth postoperative day.

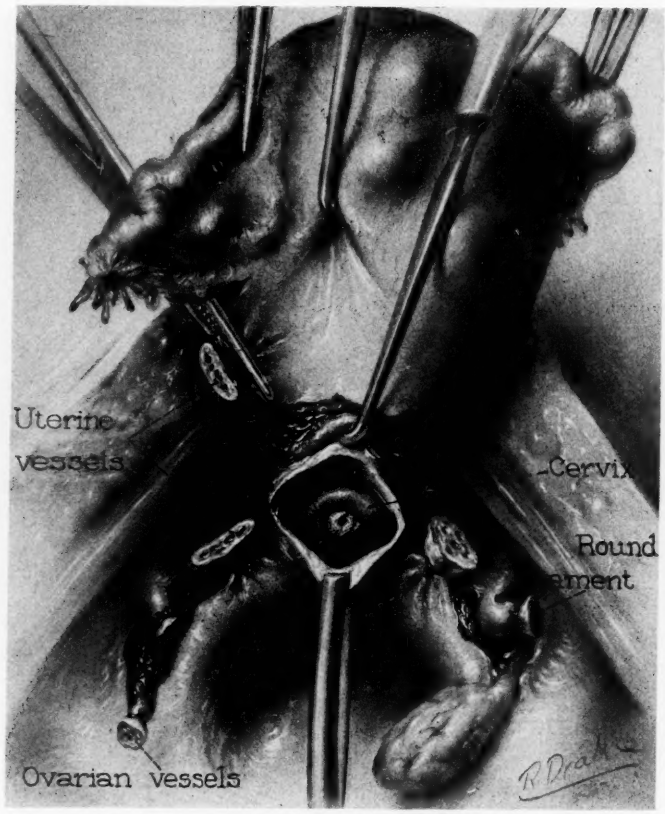

Fig. 4. The uterus freed on both sides, a hook is inserted in the posterior surface of the cervix to make traction; the vault of the vagina is cut posteriorly and a tenaculum is placed on posterior wall of the vagina; gauze soaked in tincture of merthiolate is inserted into the vagina before the operation is started.

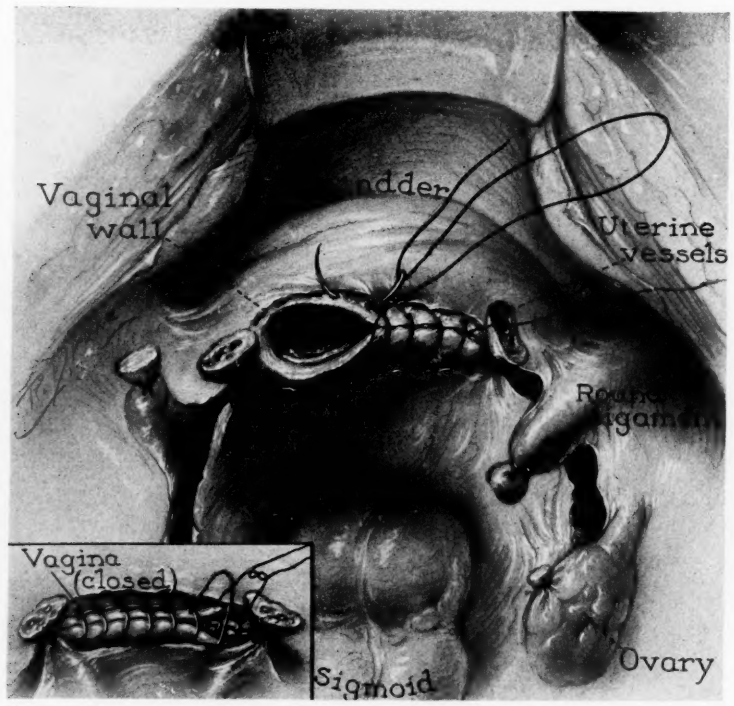

Fig. 5. Closure of vagina, showing method of insertion of two rows of sutures.

The vault of the vagina is closed with a continuous mattress suture that rolls the cut edge of the mucous membrane into the vagina and I think it is important to make a wide approximation of the round ligaments (if possible, overlapping them) to

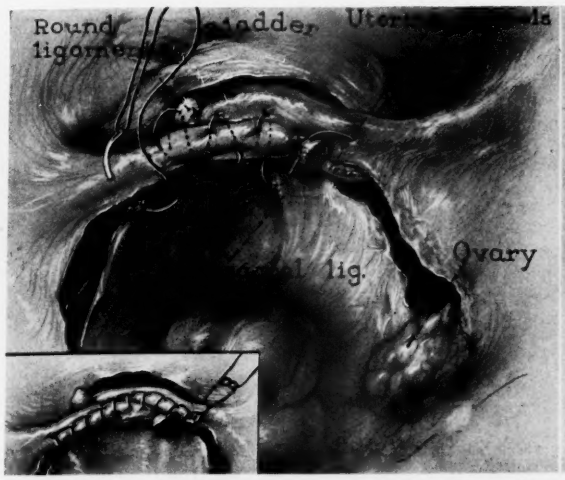

Fig. 6. Fixation by two rows of sutures of round ligaments, stumps of uterine vessels, utero-sacral ligament and vault of vagina.

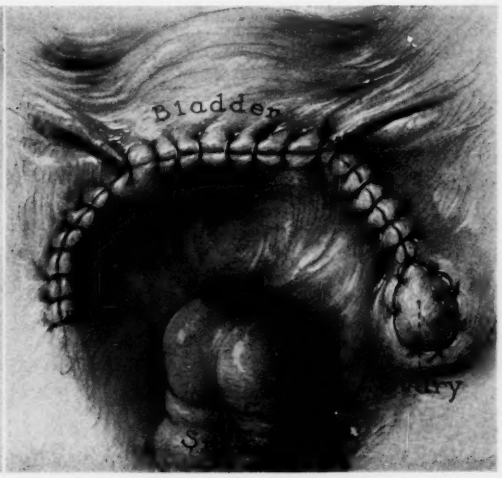

Fig. 7. Completed operation; all raw surface covered with peritoneum; ovary partially buried in peritoneum and fixed well up on side of pelvis.

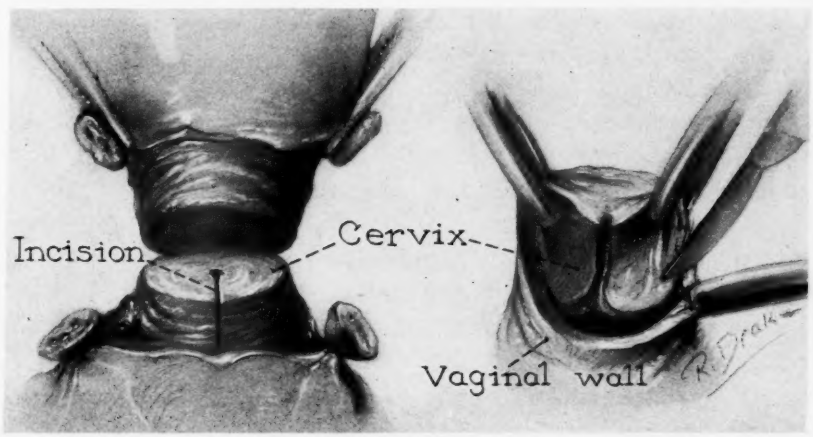

Fig. 8. In cases in which the operation is difficult the body of uterus is removed as in subtotal hysterectomy, the cervix is split posteriorly and removed separately.

vaginal canal. It is also a good hemostatic suture. To close the vagina further the peritoneum and uterosacral ligaments are brought upward from behind and placed over the vault of the vagina by a continuous suture. (Fig. 5.)

The uterine vessels and the cardinal ligament are ligated en masse by a stick tie that secures some of the vaginal wall, but an attempt is made not to reach the mucous membrane of the vaginal canal. The round ligaments are now secured to the vault of the tissues in the base of the broad ligaments, the stumps of the uterine vessels and the uterosacral ligaments. (Fig. 6.) All raw surfaces are now covered by peritoneum, and the ovary, if saved, is partly buried between the folds of the broad ligament well up on the side of the pelvis rather than fixing it to the vault of the vagina as is so often done. (Fig. 7.) If the left ovary is saved, special care should be taken to prevent it from becoming adherent to the sigmoid. If there has been an old

pelvic inflammatory condition, it is often impossible to close the peritoneum in the usual way, and it is then frequently necessary to obliterate the cul-de-sac of Douglas more or less and cover the raw surface by stitching the sigmoid and appendices epiploicae to the posterior surface of the broad ligaments and posterior surface of the vagina.

In many cases in which it is expedient to remove the cervix, especially where there is an old pelvic inflammatory condition, it often simplifies the operation to perform a supravaginal amputation first and then to split the cervix posteriorly and shell it out from the vault of the vagina under direct vision. (Fig. 8.)

In the majority of cases it is advisable to remove the appendix at the same time, as this procedure adds little if any risk to the operation and occasionally saves the patient from another intervention.

The use of drains either through the abdominal incision or through the vagina, when not necessary, is a very definite added danger to any pelvic operation and as it is seldom necessary to operate for acute pelvic conditions it is rare, indeed, that any drainage is necessary. For several years, I have never used any abdominal or vaginal drainage even in operations for old pelvic inflammatory conditions or Wertheim operations for carcinoma of the cervix. If a tubo-ovarian abscess is ruptured during removal, the pelvis is washed out with physiologic saline solution and a tube drain is carried down to the peritoneum but not into the peritoneal cavity, when the wound is being closed. There is no doubt that the peritoneum can resist infection better than the soft tissue of the abdominal wall, and if a drain is inserted into the peritoneal cavity it causes a definite increase in postoperative adhesions and in the possibility of obstruction, and no good purpose is served. Whenever an infection becomes chronic it is a definite indication that the patient has a good resistance to that particular infection.

PREOPERATIVE AND POSTOPERATIVE TREATMENT

In many cases in which there is a history of menorrhagia the patients are exceedingly poor surgical risks on account of the secondary anemia that has developed. In these cases a preoperative transfusion of whole blood definitely decreases the risk, but my practice for some years has been, if the patient is able to be up and around the greater part of the day, to have her blood typed and, if necessary, a transfusion can be given any time after the operation. Since I started using a 6 per cent solution of acacia (about twenty years ago) in any case in which the blood pressure remains low following operation or the patient exhibits any signs of shock during the operation, I have used whole blood very seldom except when the concentration of hemoglobin has been less than 5 Gm. per 100 c.c. of blood.

CONCLUSIONS

1. More than 50 per cent of women who have borne one child or more have an unsatisfactory condition of the cervix and lower part of the birth canal.
2. Statistics from most hospitals show that subtotal abdominal hysterectomy is a safer operation than total abdominal hysterectomy.
3. Experienced surgeons can develop a technique by which a total abdominal hysterectomy can be performed as safely as the subtotal operation and with a lower morbidity.
4. The bladder, bowel or ureters will not be injured if the surgeon sees what is included in the grasp of each hemostat or in each suture.
5. Danger of cancer developing in the cervical stump is not the only reason for its removal, but cancer developing at this site is more frequently reported than formerly.
6. If a total abdominal hysterectomy is properly performed there is no tendency to prolapse of vaginal vault or shortening of the vaginal canal.

7. Neglect to repair the perineum often accounts for an unsatisfactory result following abdominal hysterectomy.

8. Morbidity is most frequently due to thrombophlebitis, low-grade pelvic peritonitis and firm adhesions of loops of small intestine deep in pelvis.

9. In my opinion spinal anesthesia makes any abdominal operation easier for the surgeon but a little more dangerous for the patient.

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In 1809 Mary Crawford rode 60 miles on horseback, that Ephraim McDowell of Danville, Kentucky, might attempt the removal of an ovarian cyst so large that her abdomen hung well down towards her knees.
From—"A Textbook of Surgery" by John Homans (Thomas).

THE CHOICE OF OPERATION FOR UTERINE PROLAPSE*

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THE management of uterovaginal prolapse is a problem which has commanded the attention of gynecologists and surgeons for many years, and yet there is no unanimity of opinion in regard to the surgical treatment of this lesion. This may be proved by the fact that innumerable procedures have been proposed for the correction of this disorder. Admittedly, the problem is a complex one and no one method is adaptable to all cases. The best results, therefore, are obtained when patients are individualized and when the surgeon views the situation with an open mind, choosing the operation best suited for the particular individual under consideration.

Uterine prolapse is usually classified in three degrees: the first degree, when the cervix appears at the vulva; the second degree, when the cervix is extruded; and the third degree, to which the term procidentia is applied, when the entire uterus appears in the outside world. To a certain extent the treatment is governed by the degree of prolapse of the organs. This may be medical or conservative and surgical or radical. The medical measures are concerned with the use of pessaries and tampons, which necessarily give but temporary relief. The pessaries, however, are of value in caring for certain patients with the lesser lesions, and their employment may allow these patients to continue through the child-bearing period before resorting to operative procedures. Vaginal tamponade with gauze and lamb's wool tampons is practically never used in the modern management of this condition.

Three factors, among others, are outstanding in the determination of what operative method should be chosen in surgically treating uterine prolapse: first, the age of the patient; second, the possibility of future pregnancies; and third, as previously mentioned, the extent of the prolapse.

Extensive prolapse during the child-bearing age, because of its great discomfort, demands surgical attention. In this instance it is advisable so to reconstruct the parts that there will be no interference with future childbirth. This may be satisfactorily done by curetting the uterus, performing a bilateral trachelorrhaphy, an anterior colporrhaphy, a colpoperineorrhaphy, and, through an abdominal incision, shortening the uterosacral ligaments and performing a round ligament suspension of the uterus. The Simpson type of suspension gives satisfactory results. In this type the round ligaments are drawn through the internal rings to obliterate the spaces on the sides, and are attached to the under-surface of the anterior sheath of the rectus muscle on each side. When the round ligaments are markedly attenuated the Olshausen suspension is adequate. Here the round ligaments, close to the uterine horns, are fixed to the anterior abdominal wall by fine silk sutures. This operation has the advantage of using the strongest portion of the round ligament where it is picked up close to the uterus; it has the disadvantage of leaving a dead space on each side, but this may be overcome by closing this area with a purse-string suture of fine silk. During the child-bearing age, the cervix should not be amputated for three reasons: (1) because of the dystocia it will occasion in future labors; (2) because it is responsible for the early termination of

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pregnancy in a number of instances; and (3) because it may result in sterility. Obviously, abdominal fixation of the uterus during the child-bearing age should not be considered because of the severe dystocia which will result therefrom.

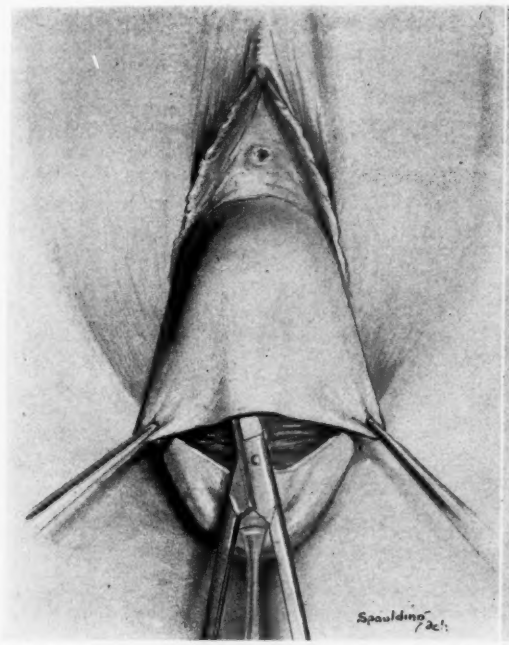

Fig. 1. The cervix is steadied by a Jacob's volsellum. A transverse incision is made in the anterior vaginal wall, in the region of the internal os. The vagina is separated from the bladder with scissors.

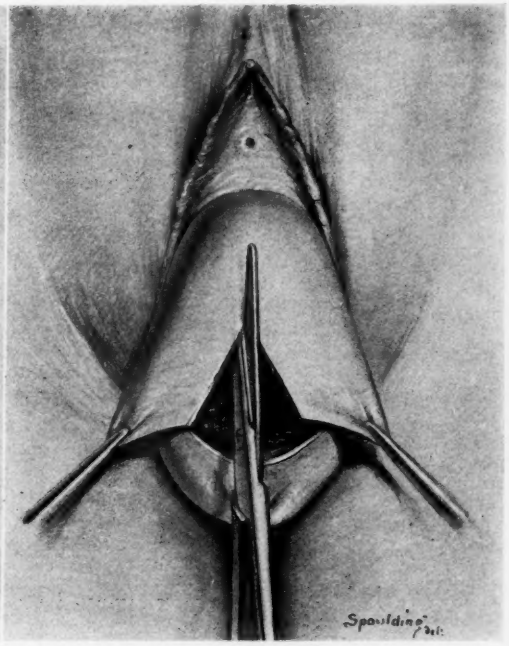

Fig. 2. The anterior vaginal wall is incised in the median line by scissors, exposing the bladder.

After the menopause, or when child-bearing is no longer a factor, certain surgeons treat uterine prolapse by amputating the cervix, performing an anterior and posterior colporrhaphy, a perineorrhaphy, and a fixation of the uterus to the anterior abdominal wall. I personally have never favored abdominal fixation in the treatment of prolapse, since, if child-bearing is not considered, I believe better results are obtained by choosing one of the methods which may be carried out entirely through the vagina. Moreover, this lessens the risk of operation, since it obviates the necessity of doing a laparotomy. Two of the largest cul-de-sac hernias which I have encountered were seen in women who had had prolapse treated by vaginal plastics and abdominal fixation of the uterus. These occurred between ten and fifteen years after operation, and, in order to overcome them, extensive vaginal dissection was necessary.

When dealing with women who have passed the menopause and with very old women, one of the vaginal procedures is usually resorted to, an abdominal incision being made only in rare instances. The reasons for so doing are that the vaginal operations increase the operability rate because of lessened morbidity and mortality; and because, in women whose child-bearing function has been terminated, the uterus and broad ligaments may be used to construct the support which elevates the prolapsed uterus and bladder in the pelvis. An adequate repair of the pelvic floor should accompany all vaginal operations for prolapse.

The vaginal operations in common use are:

1. Interposition of the uterus (Watkins-Schauta-Wertheim).
2. Vaginal hysterectomy (Mayo or Price-Kennedy).
3. High vaginal fixation of the uterus.
4. Colpectomy (Subtotal or total).

5. Interposition of the cervical stump in inversion of the vagina following supravaginal hysterectomy.

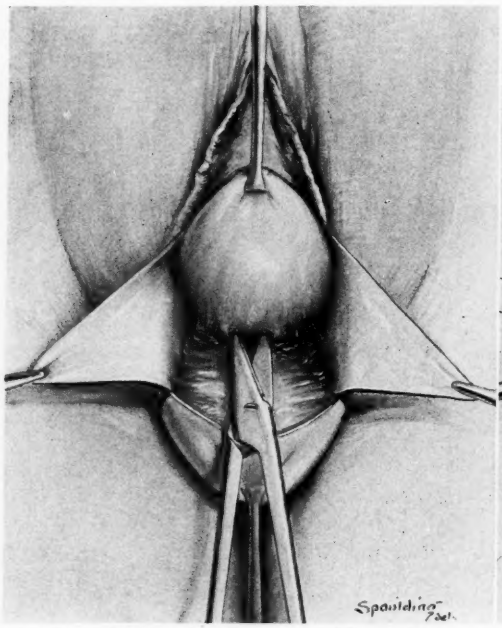

Fig. 3. The bladder is separated from the anterior vaginal wall and from the cervix by cutting the bladder pillars, thus exposing the basis of the broad ligaments.

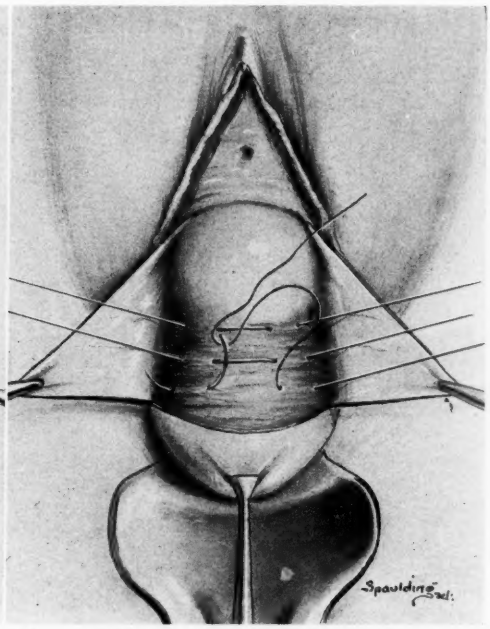

Fig. 4. Three sutures of No. 2 chromic catgut are placed in the bases of the broad ligaments and left untied.

6. Manchester operation (Donald-Fothergill).

7. Operation for hernia of the cul-de-sac of Douglas.

INTERPOSITION OF THE UTERUS

(Watkins-Schauta-Wertheim Operation)

This procedure, which was first performed by Watkins[13] of Chicago, in January, 1898, is frequently referred to in the literature as the Watkins-Schauta-Wertheim operation. Watkins performed it more than a year before Schauta or Wertheim, and should, therefore, get the credit for its establishment.

This procedure should not be advocated in women who are still in the fertile period. It is obvious that it would make delivery through the birth canal hazardous. Furthermore, if it is performed in young women, myomas of the uterus may subsequently develop, and the abnormal position of the uterus would make their treatment difficult and arduous. The operation finds its greatest field of usefulness when the uterus is normal in size, about 3 inches, (7.5 cm.) in length, and when it is not friable. It is best employed when there is a first or second degree prolapse with a large cystocele. If attempted in the presence of a senile, atrophied uterus, recurrence will be common, since the bladder, by its greater weight, will force the interposed uterus through the vulva. Again, recurrences will be more common if the procedure is used with a third degree prolapse.

A great deal has been written about the bladder disturbances which may follow this operation, but these have not occurred in my experience. If the bladder is freely separated from the anterior vaginal wall, if the uterovesical ligament and the bladder pillars are cut and the bladder is completely separated from the uterus, after the interposition of this organ the bladder will lie smoothly and not in folds on the superior and posterior surfaces of the uterus. No discomfort, as a rule, will be

encountered. If, on the other hand, the bladder pillars remain attached and the fundus of the uterus is interposed, there fact that if recurrence takes place, the organ is still present and can be utilized in an attempt to overcome the defect.

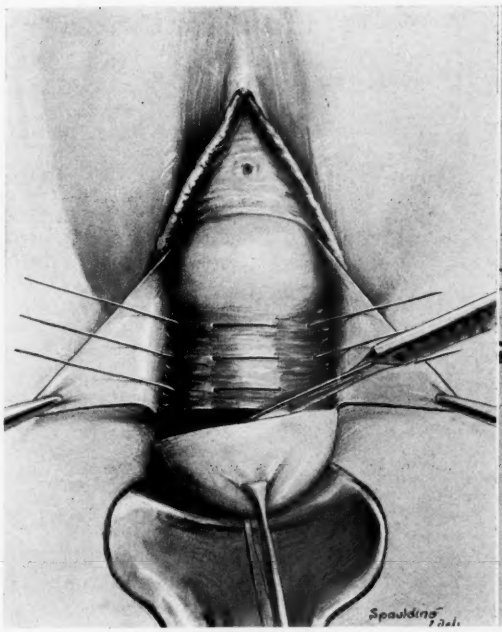

Fig. 5. The cervix is amputated below the level of the lowermost broad ligament suture.

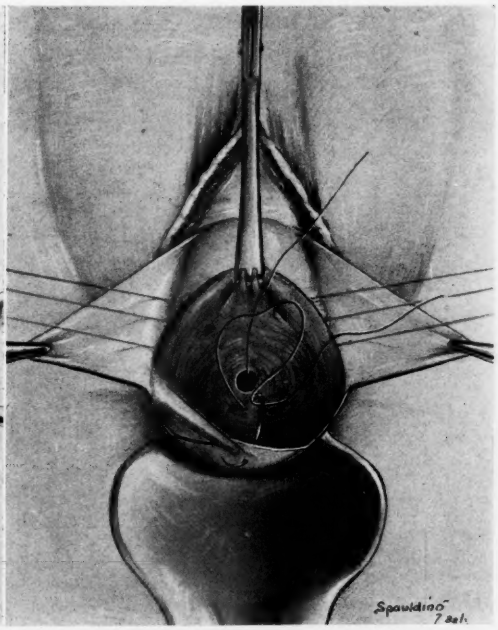

Fig. 6. The cervix is reconstructed by attaching the vaginal wall to the cervical canal, starting in the median line posteriorly.

will be constant pull on the bladder, giving rise to distressing bladder symptoms.

In my statistics of uterine prolapse and cytocele I find that I have used the interposition operation more than any other method. By observing the criteria above mentioned, I have obtained satisfactory results, although it is possible to observe late recurrences if one's patients are followed carefully. Recently I saw two women, one of whom I had observed for fourteen and the other for eleven years. Both had obtained excellent results following this intervention. However, in the course of time the uterus had atrophied, so that in each instance it became the size of an English walnut, and recurrence was noted. This recurrence can be easily corrected by performing a vaginal hysterectomy and using the broad ligaments as a support for the bladder. In the treatment of uterine prolapse, operations which retain the uterus have an added advantage in the

VAGINAL HYSTERECTOMY

(Mayo or Price-Kennedy)

Vaginal hysterectomy for uterine prolapse has been done extensively in this country during the last two decades. More recently, two clinics, the Michael Reese of Chicago[2] and the Johns Hopkins,[4] have reverted to other types of operations which conserve the uterus. In my opinion vaginal hysterectomy should be reserved for those cases in which there is uterine or cervical pathology, and in which bleeding is present. The operation may be performed with sutures or with clamps.

Vaginal hysterectomy with sutures was popularized by Charles H. Mayo. In this type of operation the entire uterus is removed, the broad ligaments are approximated and interposed between the bladder and the vagina, after resection of the excess of the anterior vaginal wall. A very important part of the intervention, and one

which is usually not stressed sufficiently, consists of the approximation of the uterosacral ligaments in their entire length by toward the urinary meatus, is resected; and the anterior vaginal wall is approximated by interrupted sutures of silkworm gut or

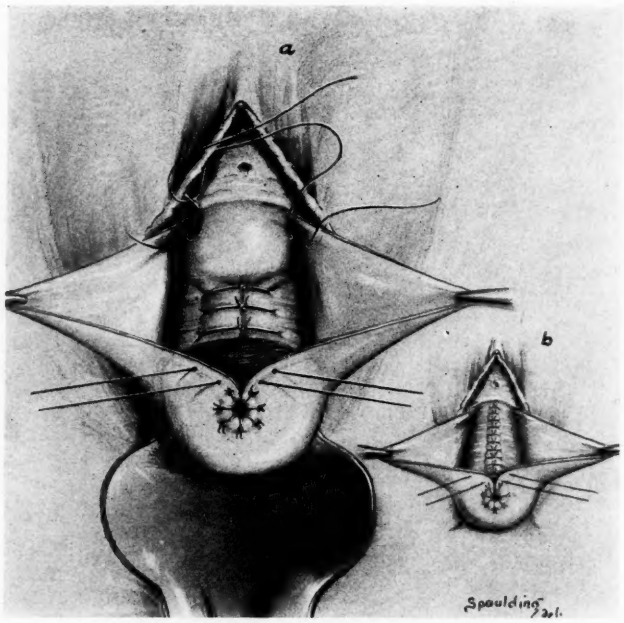

Fig. 7. *a*, the cervix has been reconstructed, the cervical canal is patent and roomy. The three broad ligament sutures have been tied. A series of interrupted sutures are placed in the musculofascial tissue, to the sides of the bladder, to overcome the cystocele. In insert, *b*, these sutures have been tied.

interrupted sutures of catgut or fine silk in order to prevent herniation of the cul-de-sac of Douglas, which frequently occurs when this condition is neglected. It is a wise plan to isolate the uterosacral ligaments, to clamp and cut them, and to replace the clamp on each side by a suture ligature at the start of operation. Like all others, this method is followed by a posterior colporrhaphy and a perineorrhaphy.

In the older group of women, when it is deemed advisable to remove the uterus in the treatment of uterine prolapse, vaginal hysterectomy may be done by means of clamps following the Price-Kennedy technique. This method is especially useful when the time element is a factor. By the use of special clamps, devised by Kennedy, the uterus may be removed in the course of a few minutes, an average time being about five minutes. Following this, a wide V in the anterior vaginal wall, with the point prepared silk. On an average this entire procedure takes less than fifteen minutes. The clamps are removed at the end of seventy-two hours, and the non-absorbable sutures from the anterior vaginal wall at the end of two weeks. Two and one-half to three weeks after the hysterectomy and anterior colporrhaphy, the perineum may be repaired. This is usually done under local anesthesia, thus dividing the operation into two stages, each stage taking but a short time to perform. This intervention is well borne by feeble women who would not stand a long operation. Its one disadvantage is that it necessitates hospitalization for four and one-half to five weeks, but this in itself is not a serious drawback when one considers the good results obtained. The results following this operation are gratifying; the vaginal vault is pulled up high in the pelvis, higher than it is possible to bring it by means of sutures, and recur-

rences are said to be very rare. I personally have not observed any during the period of time I have employed it.

In the woman who is in good condition, this method of great value in recurrent prolapse where a previous vaginal plastic operation and an abdominal fixation of the uterus had been done.

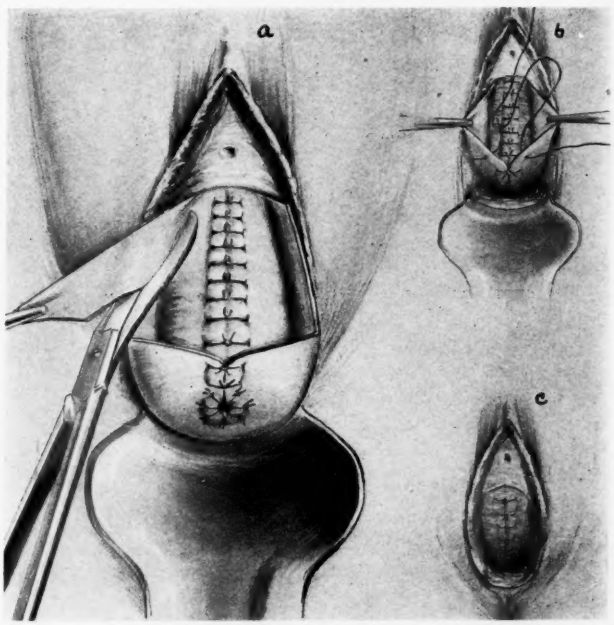

Fig. 8. *a*, the excess of the vaginal flap on each side is resected and the anterior vaginal wall is closed from below upward, *b*. The vaginal wall is entirely closed, *c*. The cervix is now well back in the pelvis, the fundus is in forward position and the cystocele has been overcome.

when the uterus has to be sacrificed, I am apt to use a modification of the Mayo technique and a colpoperineorrhaphy because the patient usually can be discharged from the hospital at the end of two weeks.

HIGH VAGINAL FIXATION OF THE UTERUS

This procedure consists of making an inverted T-shaped incision in the anterior vaginal wall, separating the bladder from the vagina and from the uterus, and suturing the anterior surface of the uterus to the anterior vaginal wall after removing, by resection, the excess of this wall. The cervix may or may not be amputated, depending upon the length of the uterus. This method raises the uterus in the pelvis and completely overcomes the cystocele. With the addition of a proper repair of the pelvic floor, adequate results in first and second degree prolapse are obtained. I have found

In a patient recently treated, the uterus had previously been fixed to the abdominal wall and the cervix appeared outside of the vulva for about 3 inches (7.5 cm.). The lower third of the uterus was amputated, the middle third was sutured to the anterior vaginal wall, while the upper third remained attached to the abdominal wall. This patient obtained a good result and has remained cured for a period of time sufficient to attest to the value of the operation. In this type of case the interposition operation or the Mayo vaginal hysterectomy are not considered, because of the increased difficulty in attempting to separate the fundus of the uterus from the abdominal wall through a vaginal incision.

COLPECTOMY SUBTOTAL OR TOTAL

Subtotal colpectomy or LeFort operation is practically devoid of shock when per-

formed under local anesthesia. It is indicated in old, feeble patients, who have a total inversion of the vagina and an atrophied uterus, or total inversion of the vagina following subtotal or total hysterectomy. It should not be employed when menstruation still exists, nor in the younger group of women. Its one drawback is that it obliterates the vagina, but this factor is not especially important in the older group of patients. It is, therefore, applicable to those whose ages make sexual congress unimportant.

For the very extensive inversions of the vagina total colpectomy, an operation proposed by Dujarier and Larget, forms a satisfactory method of treating this condition. In either case a small perineorrhaphy, approximating the levator ani muscles in the median line, forms an added barrier against recurrence. The final result is a small, shallow vagina. In my hands this operation has proved to be most successful, and considerable comfort has been obtained by the group of older patients on whom it was performed.

INTERPOSITION OF THE CERVICAL STUMP IN INVERSION OF THE VAGINA FOLLOWING SUPRAVAGINAL HYSTERECTOMY

Occasionally, one may encounter a younger woman who has had a supravaginal hysterectomy with total inversion of the vagina, including the cervical stump. Because of the age of this group of patients it is inadvisable to close the vagina, as in colpectomy. An operation which has served me well may be performed in this group. The anterior vaginal wall is opened by an inverted T-shaped incision, the vagina is separated from the bladder, the bladder is raised from the cervix, and the cervical stump is interposed between the bladder and vagina after resecting the flaps of anterior vaginal wall. A colpoperineorrhaphy is then performed. The three women upon whom I have operated by this procedure have been under observation for a considerable period of time, the results have been gratifying and there has been no interference with marital relations.

MANCHESTER OPERATION

(Donald-Fothergill)

The principle on which the Manchester operation is based consists of approximating by sutures the overstretched cardinal ligaments in front of the cervix, or the lower portion of the uterus if the cervix has been amputated. The purpose of this is to place the lower pole of the uterus backward, to elevate and antevert the uterus, these three criteria being considered essential in the cure of uterine prolapse when the uterus is retained. This is similar to the principle advocated by Alexandroff,[1] in 1903, and Tweedy,[10] in 1905.

In 1933 W. Fletcher Shaw,[9] read a paper on the subject of the Manchester operation before the American Gynecological Society, which was published in the *American Journal of Obstetrics and Gynecology*. Following this publication, the Manchester operation was taken up by several gynecologists in America, and a number of papers have appeared on the subject since that time. It is excellent for the cure of prolapse, regardless of the size of the uterus. It is well adapted to the senile, atrophied uterus. The cervix may or may not be amputated according to the length and condition of this organ. The operation is necessarily completed by an adequate pelvic floor repair. Personally, I have used this method more and more during the last few years and in cases where formerly I would have performed the interposition operation. In my hands the results have been uniformly good, and at present I am inclined to choose it in preference to any other method when the uterus is to be conserved. There is practically no shock, it can be readily performed with a small dose of spinal anesthesia, which I prefer, or with local anesthesia, and it is well supported by old women who ordinarily would not be considered good surgical risks. Because of the growing interest in

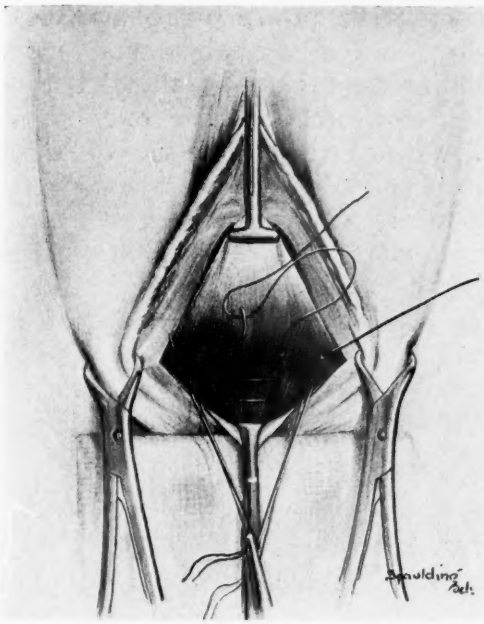

Fig. 9. The pelvic floor is opened at the mucocutaneous border the posterior vaginal wall is dissected from the rectum and the levator ani muscles and their fascia. The pelvic slings are approximated by three interrupted sutures of No. 1 chromic catgut.

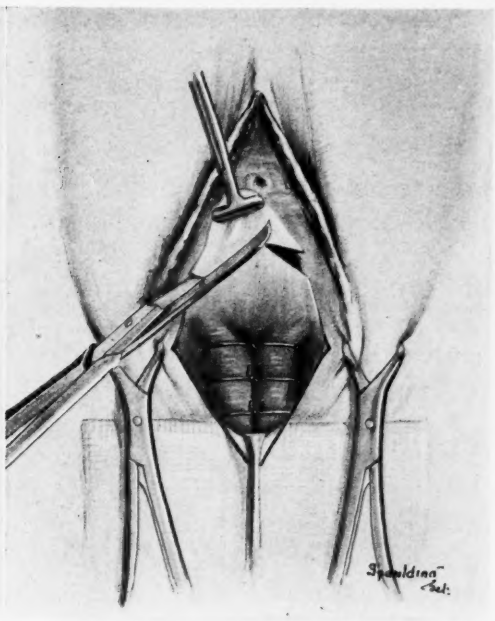

Fig. 10. The levator ani muscles and their fascia have been approximated by three interrupted sutures of No. 1 chromic catgut. The excess of the posterior vaginal wall is resected and the vagina is closed with interrupted sutures of No. 1 chromic catgut.

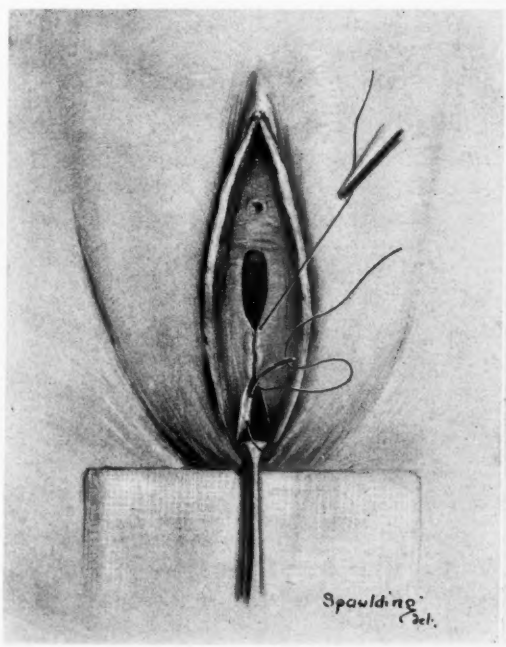

Fig. 11. Colles's fascia is approximated by a running suture of No. 0 chromic catgut.

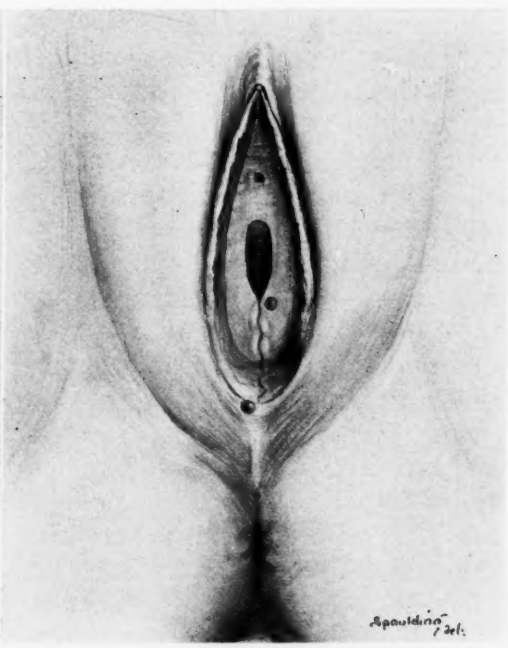

Fig. 12. The incision at the mucocutaneous border is closed by a subcuticular or a running suture of No. 0 chromic catgut, the ends of which are arrested by lead shots. In young women the vaginal introitus should be left larger.

this operation, the technique is described by illustrations accompanied by legends.

POSTERIOR VAGINAL HERNIA OR HERNIA OF THE CUL-DE-SAC OF DOUGLAS

Posterior vaginal hernia, also known as hernia of the cul-de-sac of Douglas and posterior vaginal enterocele, has received but scant attention up to recent years. In 1924, I[7] reviewed the literature of the subject and found but seventeen citations, the earliest mention being that of Marion[5] of Paris, in 1909. Formerly the lesion was confused with a rectocele. Patients were operated on for prolapse, and, if a hernia of the cul-de-sac was not discovered and repaired, there followed a mass which bulged over the recently repaired perineum as the patient assumed the upright position after operation.

In a paper read before the American Medical Association, published in 1922, George Gray Ward,[11] put this lesion on a sound basis and proposed a vaginal operation for its obliteration. Since the publication of Ward's paper, a few others have appeared in the literature. Ward's method consists of dissecting the posterior vaginal wall from the cul-de-sac of Douglas, removing the hernial sac, closing its base by sutures, approximating the uterosacral ligaments in the median line in order to obliterate the space into which the herniation had taken place, and building the perineum. The operation proposed by Marion,[5] is done through the abdomen and consists of superimposed purse-string sutures, obliterating the cul-de-sac of Douglas.

In 1912, Moschcowitz[6] proposed a similar operation in the treatment of prolapse of the rectum. His method, which is adequate for the purpose for which it was invented, is also extremely helpful in the management of cul-de-sac hernias. Most gynecologists prefer to treat these hernias through the vagina, by Ward's technique. However, occasionally one may encounter a very large hernia or a hernia complicated by adhesions, or one may discover such a lesion during the course of a pelvic laparotomy, when the abdominal method of obliteration may be thought to be the better procedure. The overlooking of a hernia of the cul-de-sac of Douglas is responsible for most recurrences in the posterior vaginal segment, when an otherwise adequate operation has been done. The bladder and uterus will usually stay up, the perineum will give good support, but the large hernia, rolling over the well repaired perineum, will be responsible for the recurrence.

Table 1

PROLAPSE OPERATIONS*

1. Vaginal plastics and uterine suspension or fixation		106
2. Interposition operation (Watkins-Schauta-Wertheim)		207
3. Vaginal hysterectomy (Mayo)		82
4. Vaginal hysterectomy (Price-Kennedy)		24
5. High vaginal fixation of the uterus		51
6. Colpectomy, subtotal, LeFort	23	
Total	6	29
7. Interposition of cervical stump in inversion of the vagina following supravaginal hysterectomy		3
8. Manchester operation (Donald-Fothergill)		50
Total		552

* There were also 40 operations for cul-de-sac hernias.

As shown by Table 1, I have personally operated on 552 women for prolapse, and on forty for hernias of the cul-de-sac of Douglas. Individualization of patients has been attempted and eight different methods have been employed in the management of this group. There were seven deaths, five after the interposition operation, and two after vaginal hysterectomy (Mayo.) The causes of deaths after the interposition operation were cerebral hemorrhage, diabetic coma, cerebral embolism, acute cardiac dilatation, and pulmonary embolism. The causes of death after vaginal hysterectomy (Mayo) were uremia, ureters patent to catheterization in one woman, and uremia in a woman whose ureters had been angulated by attaching the united broad ligaments to the upper angle of the vaginal denudation. All these deaths occurred early in the series, a number of

years ago. My last statistical paper[8] was finished in December, 1935 and published in September, 1936. Since then there has been no mortality in 170 consecutive operations of all types. The gross mortality now stands at 1.2 per cent.

In my hands the recurrences have averaged between 8 and 10 per cent. As pointed out above, these are likely to be found if the patients are followed over a period of many years. The percentage of recurrences is decreasing as time goes on, probably because of better judgment in selecting the best operation for the individual patient.

CONCLUSIONS

1. Uterovaginal prolapse in young women, during the child-bearing age, may be satisfactorily treated by repairing the cervix, the anterior and posterior vaginal walls, and the perineum, by shortening the uterosacral ligaments and by performing a round ligament suspension of the uterus.

2. After the menopause the condition may be treated by vaginal plastics and fixation of the uterus, or by methods performed entirely through the vagina. Preference is usually given to the vaginal operations on account of lessened morbidity and mortality, and on account of increased operability. In my practice an abdominal incision is made in only a limited number of cases, to obliterate a very large posterior vaginal hernia.

3. The interposition operation, Watkins-Schauta-Wertheim, followed by an amputation of the cervix, gives excellent results in first and second degree prolapse and in cases of large cystocele. Vaginal hysterectomy, with interposition of the united broad ligaments (Mayo operation) is reserved for women with atrophied uteri, and when uterine or cervical pathology is present.

4. Vaginal hysterectomy (Price-Kennedy) clamp method, finds a definite place in the management of prolapse in old women and poor surgical risks, where the time element is an important factor.

5. High vaginal fixation of the uterus, with amputation of the cervix, is useful in the first and second degrees of prolapse, with a large cystocele, and when recurrence has occurred subsequent to an abdominal fixation of the uterus.

6. In worn out and feeble old women, where an extensive vaginal operation is contraindicated, subtotal colpectomy (LeFort operation), or total colpectomy (Dujarier and Larget operation), especially when performed under local anesthesia, may render great service.

7. One or the other method of colpectomy may be used to advantage in inversion of the vagina following supracervical or total hysterectomy.

8. In younger patients who have inversion of the vagina, including the cervical stump, following supravaginal hysterectomy, interposition of the cervical stump between the bladder and the vagina may correct the condition.

9. The Manchester or Donald-Fothergill operation is an excellent procedure in cases of first and second degree, or even third degree prolapse, regardless of the size of the uterus, whether normal in size or atrophied. The cervix is usually amputated in connection with this operation, when it is elongated, lacerated or irritated. The popularity of this method has increased considerably during the last few years.

10. An adequate repair of the pelvic floor is essential in all cases, with the rare exception of cases of nulliparous prolapse, where the perineum is intact and gives good support.

11. A hernia of the cul-de-sac of Douglas, posterior vaginal hernia, should be attended to in conjunction with the repair of the pelvic floor.

12. Local and spinal anesthesia may be used advantageously in a number of these patients.

13. A total of 552 personal cases of uterovaginal prolapse and forty cases of hernia of the cul-de-sac of Douglas is reported.

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Changes [in the menstrual flow] may indicate a great variety of pathologic states. Excessive flowing may be due to fibroid tumors of the uterus, mucous polyps, a benign hypertrophy of the mucosa or adenocarcinoma of the uterine body; or again, it may result from the incomprehensible disorder known as uterine insufficiency.
From—"A Textbook of Surgery" by John Homans (Thomas).

LYMPHOGRANULOMA VENEREUM IN THE FEMALE

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LYMPHOGRANULOMA venereum now seems to be the acceptable name for a disease with so many appellations as to confuse even workers in the field of venereal disease. Four years ago we described some urethral lesions as "lymphopathia venereum,"[1] a term originated by Wolf and Sulzberger.[2] This seemed to be a superior term. However, since the Cumulative Index now lists this as lymphogranuloma venereum, the future literature should be correlated under this title. Among many other names this disease was called tropical or climatic bubo. The most widely known name in recent years has been lymphogranuloma inguinale. It was originally applied by Durand, Nicolas and Favre[3] in 1913 to chronic inguinal adenitis with multiple draining sinuses. The term was applied because of an apparent microscopic similarity with Hodgkin's disease ("lymphogranuloma").

The study of this condition progressed little or none until 1925, when Frei[4] discovered the diagnostic properties of an antigen prepared from the bacteriologically sterile pus removed from buboes. This important skin test gave impetus to world wide studies and a tremendous literature has developed. Many obscure lesions quite unconnected with the inguinal adenitis have now been brought together. The disease has been transferred to monkeys and to mice (Hellerström and Wassén,[5] and others), producing characteristic meningitis after intracerebral inoculation; to guinea pigs (Meyer, Rosenfeld and Anders[6]) producing a typical inguinal adenitis after inoculation in the groin; and to other animals. The filterable virus nature of the causative agent has been made clear by a number of investigators. It has been cultured on tissue-Tyrode media by Tamura.[7] The entity of this virus disease is undisputed at the present time.

PATHOLOGY

Gross Pathology. By means of the antigenic test inguinal adenitis has been shown to be the least important manifestation of the disease in the female. Various ulcerations of the vulva and vagina, elephantiasis of the vulva, hypertrophic rectal tags, proctitis and rectal stricture may represent different forms of the same disease. Occasional cases with extragenital or generalized lesions have been described.[8]

The primary lesion is said to begin as a small superficial ulcer lasting for a few days to three weeks. We have interpreted as primary lesions the pinkish-red puffy urethral meatus and the superficial tender pinkish ulcer occurring most often in the fourchette or extending up one side of the vestibule. These lesions may heal and disappear after a few weeks, or they may extend more deeply into the tissues, forming chronic ulcers.

The secondary forms of this disease are usually explained by the characteristic extension of the inflammation along the lymphatics. If the primary lesion occurs on the upper two-thirds of the vulva, inguinal adenitis may follow because of the lymphatic drainage. Multiple small abscesses are formed in individual lymph nodes, accompanied by periadenitis and numerous burrowing sinus tracts which connect abscesses in various lymph nodes. As the process continues a progressively increasing purulent accumulation produces a tense abscess and the overlying skin may have the bluish appearance responsible for the term "blue balls." Intense pain may accompany this, apparently because of tension in the skin.

The abscesses may rupture and form multiple draining sinuses, which are extremely indolent in healing. Following healing there is scarring and puckering about the site of the bubo. The lymphatics may be blocked in the vulva with subsequent development of chronic edema with brawny skin and secondary ulcerations. This disease explains the majority of cases of "chronic hypertrophic vulvitis."

Fig. 1. Lymphogranuloma venereum with ulcerative destruction of the anterior urethra.

If the urethra is involved, there may be only a progressive ulcerative destruction up to the internal sphincter. This feature of the disease was described by Gray in detail in 1936.[1] We have never seen a vesicovaginal fistula or involvement of the cervix.

Since most ulcers occur on the inferior third of the vulva or on the posterior portion of the vagina, the inguinal glands are not so frequently involved in women as in men, where the lymphatics of the penis and scrotum drain to the inguinal glands. In the female all variations of ulcerations may appear about the vulva and vaginal orifice. Drainage from the lower vulva and vagina extends along the rectum. The rich bed of lymphatics about the ampulla may be extensively involved in a marked lymphangitis.

In the early stages of involvement of the rectum, patients may have lassitude, low-grade fever, headache, slight deep pelvic pain and heaviness in the rectum. In such early cases there may be only tenderness on rectal examination. It seems that these might be suspected and a presumptive diagnosis made by the Frei test. If early treatment were instituted as suggested below, the late disastrous results might be averted. Apparently the infection penetrates the wall of the rectum to cause an ulcerative inflammation of the mucosa. The process may remain limited to the ampulla or extend far up the colon. These patients may lose weight, develop secondary anemia and suffer much pain accompanied by mucopurulent discharge. In later stages there is a marked scarring with contraction which produces the typical corrugated rectal stricture. The disease may extend by the lymphatics to the anus with the production of typical large elongated anal tags. The interesting recent work of Paulsen,[9] using bowel discharge and bowel tissue antigens, corroborates the identity of this form of lymphogranuloma venereum.

Fig. 2. Elephantiasis of the labia major and clitoris with ulcerative destruction of the urethra.

Whether the condition can involve the uterus and tubes is quite unsettled. The pathologic diagnosis in the Fallopian tube

is very questionable. Not infrequently the patient with rectal ulcerations and stricture may have broad ligament induration or pelvic abscess. These complications seem more likely due to extension from the rectum than to primary involvement of the upper genital tract. Cases with bacteriologically sterile pyosalpinx should be studied by animal inoculation and for antigenic effects.

Fig. 3. Elephantiasis vulvae with complete ulceration of the vestibule in a 22 year old negress. The urethra opens in the depth of the ulceration and hypertrophic tags surround the vaginal orifice.

Microscopic Pathology. A review of the pathologic studies indicates that the most characteristic microscopic findings are present in the acute or subacute inguinal bubo. D'Aunoy and von Haam[10] describe a proliferation of the endothelial cells lining the lymph spaces of the glands. Masses of large epithelial cells occur in more or less circumscribed nodules. Central necrosis with leucocytic infiltration may form characteristic triangular or quadrangular abscesses. Marked scarring of the capsule and infiltration with plasma cells follow. Many authors mention giant cells that are common and resemble either Langhans or Reed-Sternberg cells. According to D'Aunoy and von Haam, no characteristic lesions can be noted in chronic conditions.

Pund, Greenblatt and Huie[11] are very enthusiastic over the value of biopsy for the diagnosis of various venereal diseases, having determined as many as three different venereal diseases in one lesion. If this is confirmed a remarkable advance will have been made. A majority of investigators do not agree that microscopic diagnosis is as accurate as suggested by Pund and his co-workers.

In the chronic lesions there is a progressive lymphangitis frequently accompanied by chronic edema and sclerosing fibrosis of the subcutaneous and submucous tissues

resulting in enlargement and induration of the affected parts. Insufficient circulation may cause ulceration.

Edwards and Kindell[12] give an excellent description of the pathology in rectal stricture. The polypoid internal surface is made up of vascular granulation tissue infiltrated by a variety of cells. The submucosa is thickened and fibrous. Inflammatory infiltration and scarring extend throughout the muscular coats and into the fat. The accumulation of lymphoid and plasma cells is massive; in the outer coats, perivascular. Eosinophiles are scattered throughout. There are many mononuclear wandering cells. Many small abscesses or sinus tracts may contain bits of fecal material and foreign bodies with definite foreign body giant cells. Small, nodular, tubercle-like structures made up of epithelioid cells, in some containing giant cells of the Langhans type, are present in almost every specimen.

D'Aunoy and Schenken[13] found in a Fallopian tube numerous stellate abscesses surrounded by typical masses of endothelial cells from a patient with a positive Frei test. While this may be suggestive, it does not prove that lymphogranuloma venereum causes salpingitis.

We are forced to conclude that fairly characteristic but probably not diagnostic lesions occur in subacute inguinal adenitis. Other lesions are not nearly so characteristic. This is perhaps due to the marked secondary infection in the ulcerative lesions. The greatest single value of biopsy is to rule out malignancy.

A few authors have felt that these ulcerative lesions may be premalignant. Pund, Greenblatt and Huie[11] described three cases with development of epitheliomas in ulcers diagnosed pathologically as being of venereal origin. They thought there might be some causal relationship. David and Loring[14] presented two cases of long standing rectal strictures with subsequent development of squamous cell carcinomas at the site. In our experience we have never seen a case with cancer developing in lymphogranuloma venereum and believe there is no increased occurrence of malignancies due to the disease. Microscopic sections of old lesions may show marked proliferation of squamous epithelium and endothelium from the capillaries, superficially suggesting malignancy. Biopsies should be taken from all cases with chronic ulcerations, as even the experienced individual can be mistaken in a gross diagnosis.

OCCURRENCE

In recent months we have performed 326 routine intradermal Frei tests on patients at the Louisville City Hospital. Of these 127 tests were done on obstetrical patients, white and colored, and the remainder on white and colored, male and female patients on the medical and surgical wards. Our criterion for a positive reaction has been that most commonly accepted, i.e., a definite nodule measuring at least 5 mm. in diameter. The tests were read within forty-eight to seventy-two hours of their administration. In this series, twenty-seven patients (8.3 per cent) were found who had a definitely positive reaction to the Frei antigen.

Of sixty-eight tests performed on white obstetrical patients, not one was found who had a positive Frei reaction, while in fifty-nine colored obstetrical patients, only three reacted to the antigen. Conversely, in thirty-eight tests on white women admitted on the gynecologic service, four were positive, and in forty-five tests on colored patients admitted on the same service, seven were positive. This would seem to raise the question as to whether the lymphogranuloma venereum does produce some degree of sterility or whether the type of patient ordinarily seen suffering with lymphogranuloma venereum is the sexual derelict prone to all the diseases of the reproductive system and not given to child-bearing.

In a series of 183 routine Frei tests on colored gynecologic patients previously done by one of us (L. A. G.) at the Johns

Hopkins Hospital in Baltimore, forty-one (22.4 per cent) were found who reacted positively to the antigen. Comparing these results with those obtained on a similar group at the Louisville City Hospital, where 15.5 per cent positives were found in forty-five colored gynecologic patients, it would seem that the history of the disease is substantiated; that is, that the progress of the disease is from the seacoast inland, and that the incidence in Louisville may for this reason not be as great as it is in Baltimore.

Of the twenty-seven Louisville patients reacting positively to the antigen, twenty-one gave a history compatible with the infection and six denied knowledge of ever having experienced any evidences of the disease. The interval of time that had elapsed between performance of the test and the date of the disease as given by the patient varied from a few weeks to twenty-nine years. Dmelcos and Ducrey tests were performed at the same time as the Frei test, and in each case of a positive history either the test for lymphogranuloma venereum or for chancroid was positive. Of the forty-one who gave positive reactions to the Frei antigen in Baltimore, twenty-six gave positive histories while in fifteen there was no definite history to indicate existence of the infection.

It is extremely important to bear in mind when using the Frei or allied skin tests, that all but a very small percentage remain positive for life unless the patient has been desensitized. Occasional cases with negative tests may be due to anergy or lack of allergy. It also seems likely that the tests will not produce a positive reaction until an interval of two or three weeks after the infection. The Frei test would appear indispensable in the diagnosis of patients with venereal disease. The interpretation of results must be carefully integrated with a complete understanding of the clinical manifestations of the disease and the reading of the test.

The present methods of securing and preparing the antigen makes it impracticable for the use of the individual practitioner, but certainly no gynecologic or venereal clinic should be without it. Refinements that are being made in the mouse brain antigen (removal of the factor of sensitivity to the mouse brain itself) seem likely to make a reliable commercial product available in the not too distant future.

TREATMENT

The methods of treatment of lymphogranuloma venereum have been so many and varied as to suggest immediately that none of them are of any great value, but recently we have been given reason to hope for better results.*

The use of Frei antigen as treatment, in our hands, has seemed to be efficacious. We have experimented rather widely with its use both intradermally and subcutaneously. Of the two methods, the intradermal route is distinctly the method of choice. Using intradermal injections, two, or preferably three times a week, one may expect a subsidence of the majority of lymphogranuloma venereum buboes that are not well along toward suppuration, within two to three weeks. Patients with rectal stricture complaining of great amounts of rectal discharge (sufficient to necessitate the constant wearing of pads), have invariably volunteered the same information, i.e., within a few days after being started on the treatment their discharge has increased very perceptibly in amount, but become quite thin in character. After a period of ten days there has been a noticeable checking of the flow until within a month all who continued on the regimen were able to discard the pads. They further have reported loss of sensation of heaviness in the rectum and an increased feeling of well-being. Many patients who previously had been subjects for repeated manual

* This work has been done in the Genital Lesion Clinic of the Louisville City Hospital under the direction of one of us (M. L. B.) and in close coöperation with the Departments of Dermatology and Bacteriology. A more detailed report will be made in the near future.

dilatations of the rectum at ever diminishing intervals, have found that the intervals were considerably lengthened while on treatment.

The use of the antigen as treatment has given good results with the primary chancre of lymphogranuloma venereum occurring in the vaginal fourchette. Of three cases with persistent lesions of the female urethra, two were completely cleared up with the use of the antigen. The third was resistant to all therapy, including sulfanilamide, but improved remarkably following prolonged administration of antigen.

Recently sulfanilamide has been introduced for the treatment of lymphogranuloma venereum. This drug seems to hold considerable promise for therapy of this condition. To date we have had only six cases of buboes progress to suppuration during the course of the administration of this drug. On questioning, four of these patients have frankly admitted failure to keep up an adequate dosage of the drug. The use of sulfanilamide seems to be of benefit to the patient with rectal stricture or those with a persistent primary. Whether its action is on the virus or on the secondary pyogenic invaders, as suggested by Torpin, Greenblatt, Pund, and Sanderson,[15] we are unable to say. Results from the use of this drug in the treatment of lymphogranuloma venereum are certainly far short of its rather miraculous effect in the therapy of chancroidal lesions and chancroidal buboes. In the treatment of lymphogranuloma venereum buboes, the swelling and pain are reduced considerably within a few days, but in our experience one may expect an interval of several weeks for the complete subsidence of enlargement of the glands. One feature has struck us rather forcibly. Whereas previously in this institution fluctuant lymphogranuloma venereum buboes were quite prevalent, in recent months they have become almost a rarity. In reviewing this incidence we find that it coincides almost precisely with the date when sulfanilamide first attained its very widespread use, both in our clinics and by private physicians, in the treatment of gonorrhea and other diseases.

We do not know how long a patient may retain the ability of infecting others or in just what stage the disease must be in order for the infection to be transmitted. It seems to us theoretically possible that the general use of the drug is either eliminating many of the sources of infection or is serving as a prophylactic agent while being used as therapy for other conditions.

In the treatment of chronic hypertrophic vulvitis, vulvectomy should be performed only when the suture line joining the vestibule is free of ulceration. Otherwise it is likely to separate widely with the formation of an encircling ulceration slow to heal and prone to severe hemorrhage early after operation. The results are most gratifying where the suture line is clean.

In many cases with stricture of the rectum and marked ulceration with bleeding and discharge, sigmoidostomy is followed by general improvement and abatement of the local symptoms. Occasionally the inflammatory process may ascend to the colostomy opening, causing stricture and necessitating additional higher colostomies. In these cases, however, there is usually some involvement at the time of operation in the original colostomy. Warthen[16] has suggested an operation by which the lower pelvis is closed off from the upper abdomen by peritoneal sutures before the colostomy is performed. Subsequent dilatation of the rectum is thought to be less dangerous in producing generalized peritonitis. Edwards and Kendall[12] have had good results in excising the rectum by the Lockhart-Mummery method.

SUMMARY AND CONCLUSIONS

Lymphogranuloma venereum is a well proved virus disease entity. Further variations in this disease will undoubtedly be found. The new concepts developed within the past fifteen years have gone far to clear up the confusion of many lesions in the female. One phase of diagnosis and treat-

ment should command the attention of every practitioner, namely: the zealous attempt to recognize and treat the early stage of rectal stricture. We believe that the acute involvement of the glands of Gerote must be accompanied by a fairly definite group of symptoms which may lead to a diagnosis substantiated by the Frei test. Intense treatment by Frei antigen, sulfanilamide or a combination of the two, may avert the eventual addition of another semi-invalid to a group already too frequently seen, particularly in the southern Negro female.

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VAGINAL HYSTERECTOMY—ITS INDICATIONS AND TECHNIQUE*

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VAGINAL hysterectomy is not a new procedure. Our grandfathers in gynecology, the founders of our special societies, were thoroughly familiar with its technique and indications. When, however, "perityphlitis" was found to be appendicitis and operation promised much in its cure, then the surgeons began to invade the abdomen for "chronic" appendicitis. While inside they discovered Jackson's membrane, cecum mobile, and a number of other anatomic deviations, and placed much stress upon their correction. Then gynecologists became enthused over this new surgery and departed from their vaginal technique in order to combine their indicated pelvic work with these new operative wrinkles. In consequence, vaginal surgery became neglected and recently one could find busy clinics where not a single vaginal hysterectomy had ever been performed either by the present staff or by their predecessors. Since the prophylactic surgery described above is known now to be meddlesome and frequently harmful and since the vaginal approach to pelvic disease is associated with less mortality, a smaller morbidity rate and a much more rapid convalescence, it is high time that present day gynecologists learned to appreciate the value of vaginal hysterectomy, acquire its technique, and extended its use.

In vaginal surgery, because of the restricted field, more delicate instruments are necessary than in abdominal work. A retractor a little too wide may make difficult an otherwise easy operation. The operating table should be such that when the patient is in the lithotomy position the pelvis is in the proper plane, tipped neither too far upward or backward. A good spotlight thoroughly to illuminate the operative field is indispensable.

The beginner in vaginal surgery would do well to select his first cases for vaginal hysterectomy with considerable care, picking out easy cases until, as his skill increases, he may elect to do more difficult ones. The vagina should be roomy enough to allow the necessary manipulations. A narrow introitus can be overcome by a small episiotomy incision. A vaginal vault which is poorly developed or constricted will cause great difficulty. On the other hand, it may be easier to operate upon a nullipara than upon a multipara with too roomy a vagina, where the walls may fall together laterally and obscure visibility.

The uterus should not be too big. The first cases should allow the uterus to be delivered intact so as to allow prompt recognition of its upper attachments. When more experience has been obtained a uterus a little too large may be divested of its cervix to allow its removal. Later when one has learned to recognize the round ligaments and the attachments of the tubes and ovaries under all conditions, tumors of large size may be tackled for morcellation. The larger the tumor, however, the greater the chance of running into unexpected pathology in the appendages or the uterus itself.

The uterus should be freely movable. Fixation may be due to previous pelvic infection, so that the uterus may be surrounded by adhesions, and the appendages may be fixed and inaccessible, or it may be due to malignancy and the uterus be irremovable. A vaginal hysterectomy may

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be safely done in spite of this contraindication but it may call for much dexterity and caution on the part of the operator.

The operation should not be attempted if the patient has had previous pelvic surgery, especially by laparotomy. Adhesions of the intestine to the uterine body or appendages commonly form even after attention by experts. If these are encountered, sharp dissection with care to leave a bit of the uterine tissue on the intestine instead of the reverse, is usually easy, though one must be prepared to suture quite promptly any injury made to the intestine. Before transgressing this contraindication, one should rule out by careful history-taking, the probability of a previous intestinal obstruction, because there may be loops of intestine adherent to the old abdominal incision which cannot be loosened by the vaginal route, and which may precipitate an obstruction during convalescense due to overdistention of the guts. Particular attention should be paid as to whether there has been a previous uterine fixation or such an operation as might result in fixation. If this is encountered anyway, careful boldness may solve the difficulty. One should not work blindly; if reasonable headway is not made, then the cervix should be cut off, bleeding points sutured, a large pack introduced into the pelvis to press against the uterine body, the vaginal vault closed carefully, the abdomen opened and the operation completed. I have had to desert the vaginal route and proceed abdominally only twice and in both instances the necessity arose because of a previous fixation of the uterus. In either case was the recovery any different than would be expected after the usual laparotomy.

If vaginal hysterectomy has been decided upon, the patient, after the usual preparations, is anesthetized with ethylene gas and when asleep is placed in the lithotomy position. After thorough cleansing of the vagina and vulva with soap and water, the vagina is well but gently swabbed with Lugol's solution and the bladder emptied by the use of a catheter.

The cervix is grasped with a bullet forceps and pulled down as far as possible. If, in spite of previous cauterizations, the cervix does not seem free of infection it is thoroughly cauterized again at this time. An injection of 2 c.c. of obstetrical pituitary extract is given into the paracervical tissue so as to make the operation as bloodless as possible. A transverse incision is made through the mucosa anteriorly, below the attachment of the bladder. If there is doubt as to how low the bladder lies on the front of the uterus a sound may be introduced into the bladder to determine this point. The anterior wall of the vagina with the attached bladder is then separated from the anterior wall of the uterus. Sometimes this proceeds easily by use of the gloved finger or with gauze, but frequently sharp dissection is necessary. At any rate, one must keep rather towards the uterus than towards the bladder. If, in spite of care, the bladder is unavoidably entered, the mucosa should be sutured with interrupted No. 0 chromic catgut and the muscularis similarly sutured over the mucosal row. After the operation a retention catheter is placed in the bladder, to be removed when the patient is allowed out of bed. If the plica vesicouterina is easily found, it is incised and a narrow bladed retractor inserted into the peritoneal cavity. If an anterior repair is to be made or a prolapse corrected, before the peritoneum is opened, the bladder is freed from its attachments to the anterior vaginal wall up to the anterior urinary meatus. If a prolapse is being operated upon or if urinary incontinence exists, the entire length of the urethra is exposed and the fascia lying to each side of it is brought together over the urethra with two or three No. 1 chromic catgut sutures. The vaginal mucosa is then closed with the same sutures over the urethra. The removal of the excess vaginal mucosa and the completion of the anterior repair is postponed until the uterus has been removed.

If the plica vesicouterina is not promptly found the search is abandoned and an approach to the posterior cul-de-sac is started. A transverse incision is made through the mucosa posterior to the cervix at the height of the posterior vaginal fornix. The mucosa is pushed backwards to expose the peritoneum which is incised and a narrow bladed retractor is inserted there. Occasionally the posterior cul-de-sac is also not easy to enter. Instead of wasting time and unduly traumatizing the tissues, one then proceeds to the loosening of the uterus from its attachments. The anterior and posterior vaginal mucosa incisions are united by a lateral incision on each side of the cervix and the mucosa pushed back about ⅛ inch on each side. Whether the peritoneum has been entered or not, the sacrouterine ligaments are now clearly exposed. The left sacrouterine ligament is firmly clamped with a slender curved clamp, the ligament cut on the uterine side and the clamp replaced by a No. 2 chromic catgut fixation ligature, which suture material is used throughout the rest of the operation. In the same way the exposed portion of the lower end of the broad ligament immediately above the sacrouterine ligament is similarly clamped divided and ligatured. If one was successful in entering both the anterior and posterior cul-de-sacs as in the uncomplicated technique, then if both retractors are held strongly apart and to the left side, the uterine vessels can now be seen, clamped and ligated without fear of interfering with the ureters. If neither cul-de-sac has been entered, as soon as the left sacrouterine ligament has been clamped, incised, and ligated, the right sacrouterine ligament should be similarly disposed of. Severing both sacrouterine ligaments allows the uterus to be pulled further down. If not previously possible, the posterior and anterior cul-de-sacs should now be possible of entry. When both uterine vessels have been clamped and loosened the uterus can be still further drawn out. Ordinarily at this stage, the body of the uterus presents at the posterior opening and by the use of bullet forceps can be delivered into the vagina, the fundus down. The upper part of the broad ligament is clamped and disposed of, as was done with the lower portions of the broad ligament, except where the sacrouterines were left with a double strand of catgut to identify them; the upper portions are left with a long single strand attached. The first clamping of the upper end of the broad ligament usually includes the suspensory ligament of the ovary, the uterine end of the Fallopian tube and the round ligament. The rest of the broad ligament is freed by clamps and fixation sutures, and the opposite side is then similarly attended.

When the uterus is somewhat too large for delivery intact, the cervix may be cut off just below the ligated uterine arteries, which reduction in size usually allows easy delivery of the uterine body. If the remaining mass is still too large, as much as possible is to be excised, either by a long handled scalpel or sharp scissors, in a succession of morcellations until the entire uterus can be delivered. This should be done under full vision, and before each chunk is removed the remaining portion should be fixed in position with a bullet forceps to prevent retraction and to control bleeding. As early as possible during a morcellation the upper portion of the broad ligaments should be identified, clamped, and tied off, for with both uterine vessels already tied off there need be no fear of excessive bleeding after the ovarian vessels are securely ligated.

The appendages are now to be inspected. Pull down on each of the single stranded ligatures until the knot is visible, then seize the stump with a long Allis forceps and bring down the appendages and inspect for possible pathology. Occasionally pathology is encountered which is difficult of removal, in particular, adherent inflammatory adnexa. Such appendages can be loosened by gentle manipulation with the fingers, just as is done in abdominal operation. If the uterus has not been easily removed, especially if pedunculated fibroids were present, and particularly if morcella-

tion was necessary, then after the appendages have been disposed of, all instruments should be removed from the operative field and two fingers inserted through the vaginal vault to feel for possible uterine remnants since a pedunculated fibroid may have been peeled off the uterine body and left behind. Unless an intraligamentous nodule has been left such nodules are easily removed; if intraligamentous, more exactness is required.

All ligatures should now be inspected and hemostasis perfected. The pelvis is now ready for closure. If an anterior repair is to be done, the anterior vaginal flaps are excised and any spurters found are isolated and separately ligated instead of depending upon a running suture. If the patient had a prolapse the round ligaments are caught, each with a long Allis forceps as high up as possible. A chromic or silk suture is passed through the vaginal mucosa to the left of the vaginal flap just below the last suture used in covering the urethra after the urethroplasty. It is passed through the mucosa and a good bite of the lateral vaginal fascia is included; then it is passed around the round ligament as high up as possible on the left, and a similar bite is taken through the right round ligament. The suture then passes through the right vaginal fascia close below the internal urinary meatus and out through the mucosa close to the medium incision. This suture is then carefully but firmly tied. This step anchors the round ligaments under the urethra and brings the bladder to rest upon the broad ligaments. When this is done, a couple of interrupted sutures will unite the broad ligaments together in the midline. If silk is used for the anchoring of the round ligaments its removal must be delayed until three or four weeks after the operation. Whether a prolapse operation is being performed or the patient is to have an anterior repair completed, interrupted sutures close the incision from the urethral area up to the vaginal vault.

The vaginal vault is then closed. A small pack is inserted to keep the intestines back. A suture is passed through the right edge of the anterior vaginal cuff which takes several superficial bites of the denuded surface of the bladder and then picks up the anterior fold of the peritoneum. The ligature holding the upper portion of the broad ligament is drawn down, to expose the peritoneal fold running from the bladder to the broad ligament. The suture takes bites of the peritoneum until it reaches the broad ligament, where it is passed around the tubo-ovarian stump in order doubly to ligate the ovarian vessels. The suture now picks up the peritoneum of the broad ligament in successive bites until it reaches the stump of the uterine vessels and sacrouterine ligament, around each of which it is passed that these areas may be ligated again. The suture is passed through the right edge of the posterior peritoneal flap, through the vaginal wall and out into the right side of the posterior vaginal fornix. This suture, when tied, has anchored the broad and sacrouterine ligaments to the vaginal vault, doubly ligated the ovarian and uterine vessels, has performed a peritoneal toilet and has closed the right side of the vaginal vault. The left side is now similarly treated. Before tying this suture, if a deep cul-de-sac is present or if a prolapse is being treated, a suture is taken which ties both sacrouterines together and obliterates the cul-de-sac. The rest of the vaginal vault is closed with two or three interrupted sutures.

A posterior colpoperineorrhaphy is done if indicated. If the bladder has been injured, a urethroplastic operation is performed, or, if an extensive anterior repair has been done, then a hollow tip Mallencot two-wing rubber retention catheter is inserted into the bladder to be left there until the patient sits up. When the time comes for its removal the catheter is cut close to the urethra, the edge of the catheter is held by an artery forceps and a sound pressed into the catheter to lengthen the head, so that it may be withdrawn without dilating the urethral wall. After an ordinary hysterectomy the bladder is

emptied by a glass catheter and a vaginal pack is inserted to support the vaginal vault during coughing or vomiting. This pack is removed after twenty-four hours. The same attention is given the bladder as after abdominal hysterectomy.

On the seventh postoperative day perineal sutures, if present, are removed and the patient is allowed out of bed. The average length of stay in the hospital is twelve days.

This operation can be performed with a mortality of ⅓ per cent in a series of several hundreds of cases, not excluding any as poor surgical risks but including delicate old women, a considerable portion of morcellations as well as nulliparae and virgins with intact hymens. The technique is not difficult. Anyone who can do an interposition operation nicely should have no particular difficulty in doing a vaginal hysterectomy well. A skillful gynecologist should be expected to perform every operation in his very restricted field. No operation, under certain conditions, can be more strictly indicated than a vaginal hysterectomy and frequently no other operation can be fairly substituted for it.

Since the various genital organs have a very limited number of responses to disease, any one symptom may represent a considerable number of pathological states, some of them very dangerous and others relatively harmless.

From—"A Textbook of Surgery" by John Homans (Thomas).

CAUSES OF POSTMENOPAUSAL BLEEDING*

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THE development of modern gynecology may be divided into three eras. In the first, the pioneers ventured into and made great progress in operative technique. Those early surgeons soon brought to light an abundance of pathologic material which was carefully studied in the laboratories of the better clinics and thus a new era of cellular pathology, as applied to gynecology, was developed. The pathologists did much toward explaining the causes of uterine bleeding, but there were many cases in which both gross and microscopic studies of the tissues failed to explain adequately the bleeding.

While the development of operative technique and pathology was in progress some attempts were being made to understand the physiology of the sex organs. Some of this early work, such as that of Fraenkel, on the function of the corpus luteum, was of fundamental importance and has been amply substantiated by later workers. But most of our knowledge of sex physiology has developed from the work of the past fifteen years. This newer knowledge of physiology marks the third era in the development of gynecology. It is natural that gynecologists should attempt to utilize this knowledge to understand those cases of bleeding which were not satisfactorily explained on the basis of organic pathology. These attempts have given us some incomplete understanding of functional uterine bleeding. During and before the menopausal years this group is a large and important one but after the menopause an organic lesion can be found in almost all cases of bleeding. This is not to say that physiology has no place in the consideration of postmenopausal bleeding, for it has an important bearing in many cases. Nevertheless, even in those cases in which there is an important physiologic factor an organic lesion is usually demonstrable as the actual cause of bleeding.

Some years ago we made a clinical and pathologic study of the causes of bleeding after the menopause. We studied the pathologic material and clinical cases occurring in the Johns Hopkins Hospital between January 1, 1919 and January 1, 1935. Our findings have been a constant reminder to us that the appearance of blood from the genital tract after the cessation of the menstrual life is a symptom which should never be considered lightly. A complete examination to locate the lesion responsible for the bleeding should never be deferred, for our findings indicate that the lesion responsible for the bleeding is usually a serious one and delay in treatment may take away from the patient her only chance of cure.

The most frequent lesion which we encountered was cancer of the cervix which occurred in 32.4 per cent of the cases. Cancer of the body of the uterus occurred in 14.9 per cent. The combined incidence of the two types of cancer of the uterus was 47.3 per cent. This figure, however, does not represent the total incidence of malignancy in the generative tract causing bleeding after the menopause. To it must be added the following: 3.1 per cent, representing the cases of malignant ovarian tumor; 1.4 per cent, representing cases of sarcomatous change in myomata; 0.9 per cent, representing the cases of sarcoma of the endometrium; 0.3 per cent, representing one case of sarcoma of the vagina; and 0.3 per cent, representing a case of carcinoma of the vagina secondary to carcinoma of the rectum. The total incidence of malignancy in our cases of bleeding from the vagina after the menopause is thus

* From the Gynecological Department, Johns Hopkins University.

brought up to 53.3 per cent. (Fig. 1.) Our figures are in keeping with those found generally in the literature, the incidence of malignancy in most series being in the neighborhood of 50 per cent and in a few series considerably higher.

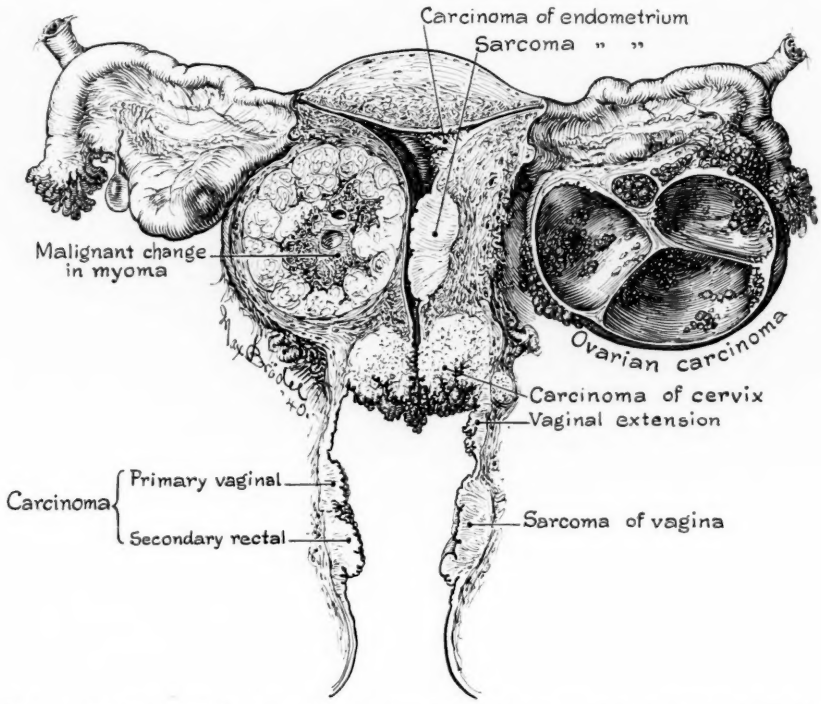

Fig. 1. Diagrammatic chart illustrating malignant causes of postmenopausal bleeding.

Stated as simply as possible, this means that a woman presenting herself with bleeding after the menopause has a greater than even chance of having malignancy. If the profession at large could be made to realize this single fact more women would be brought to treatment relatively early and many more cures could be effected. This is particularly true of the group with carcinoma of the body of the uterus. With cancer of the cervix, bleeding may occur early but all too often a rather extensive intracervical lesion is present before there is sufficient bleeding to attract the woman's attention. Fortunately, with cancer of the endometrium the growth begins in the delicate endometrial tissue which bleeds easily. Then, too, endometrial cancer starts in the center of a relatively free lying organ which can easily be removed with an excellent chance of cure if the lesion is detected reasonably early.

Since malignancy was responsible for bleeding in 53.3 per cent of the cases, there remained a large group of cases (46.7 per cent) in which a benign lesion accounted for the bleeding. (Fig. 2.) Cervical ulceration due to prolapse accounted for the bleeding in 10.7 per cent of the cases. This lesion is obvious on inspection and its benign nature is usually apparent. If any doubt exists biopsy should be done if one contemplates an operation for the prolapse such as the interposition or Manchester operation in which the corpus of the uterus is to be saved. A curettage should also precede these operations to exclude, with certainty, a malignancy higher in the uterus.

In a considerable group of cases of slight bleeding after the menopause, postmenopausal vaginitis is responsible for the symptom. In our group the incidence was only 6.9 per cent, but the cases which we studied were all hospital admissions. In the majority of cases of vaginitis the lesion is obvious on speculum examination and the

cases are treated in the dispensary or physician's office. Hence, this small percentage is not a true index of the incidence of this lesion. After the menopause, when the estrogenic hormone is withdrawn the effect of this is usually readily noted on the vaginal mucosa. The rugae become smooth and the epithelial lining becomes much thinned. In the sexually mature woman prior to her menopause the stratified squamous epithelium is 25 to 50 cell layers deep. The mucosa is a dull pink in color due to the heavy epithelial layer covering the blood vessels. This epithelial layer protects the subadjacent tissues from infection. After the menopause the epithelial wall of the vagina is much reduced in thickness. Consequently the blood vessels lying beneath the epithelium give the vagina a redder color. This thin epithelium is easily subject to abrasion and the small abrasions serve as portals of entry for the ever-present vaginal flora. Vaginitis results and produces a discharge which, because of the abrasions, is often blood tinged. Not infrequently in elderly women, in whom sexual intercourse is rare, adhesions form between the abraided, collapsed vaginal walls. The rupture of these adhesions at coitus or on exertion may on occasion cause bleeding which, at times, is quite profuse. This bleeding can be frequently demonstrated in the office by breaking the adhesions digitally.

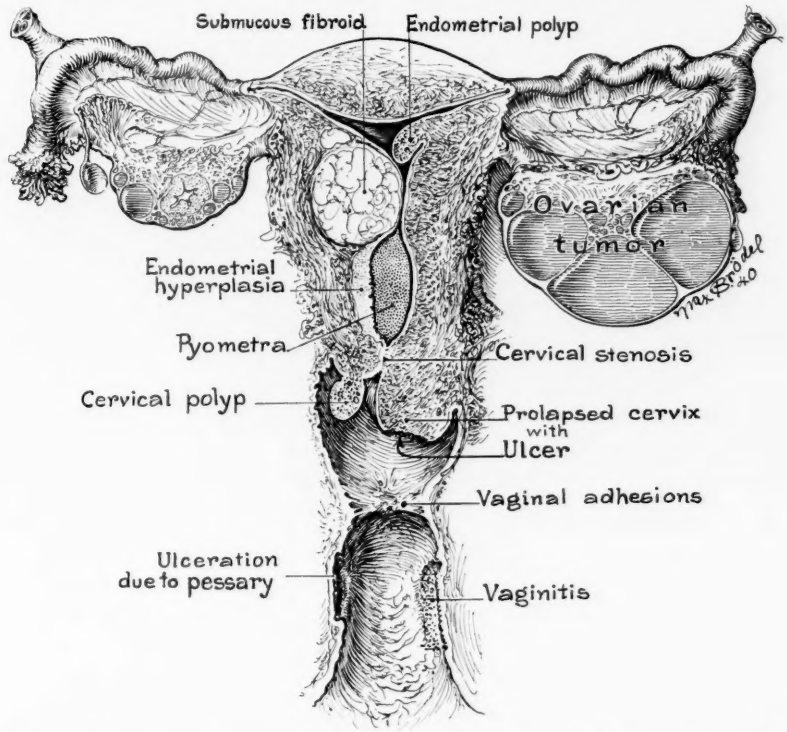

Fig. 2. Diagrammatic chart illustrating benign causes of postmenopausal bleeding.

Cervical polyps were responsible for postmenopausal bleeding in 6.6 per cent of the cases. Such polyps are no respector of age. We have never seen one before the beginning of menstrual life, but they do occur at any time before the menopause and also after it. They invariably become infected and often ulcerated. The spotting which frequently appears after coitus or on straining is rather characteristic of an ulcerative lesion on the cervix and often is the first sign of cervical cancer. The finding of a polyp after obtaining such a history is indeed fortunate. All cervical polyps should be removed and biopsied, but the incidence of carcinoma in them is very rare. They are frequently the site of epithelial metaplasia producing cancer-like lesions. A follow-up

study of a group of these cases has proved to us that they are benign. Their greatest importance lies in the necessity of their recognition as benign lesions and in thus preventing unnecessary radical surgery. I am convinced that hundreds of panhysterectomies are done annually in the United States because of erroneous interpretation of these microscopic pictures.

Cancer-like epithelial changes are not limited to cervical polyps. With the profession becoming more "cervical inspection conscious" more biopsies are taken and hence more of these suspicious lesions are seen. Their proper interpretation becomes increasingly important with their increasing number. It is not within the scope of this paper to elucidate the finer histologic changes. Suffice it to say that every bit of tissue removed from the cervix for diagnosis should be examined by a competent gynecological pathologist, bearing in mind that many competent general pathologists are not expert in the gynecological field.

Endometrial polyps also occasionally occur after the menopause and cause bleeding. A curettage usually stops the bleeding, at the same time establishing a diagnosis. A polyp, however, is often brought away so minced up that it cannot be recognized as such in the curettings.

Endometritis occurring after the menopause may be responsible for bleeding from the atrophic uterine mucosa. The cause of the infection is not always apparent but in many cases a definite stenosis of the cervical canal can be demonstrated. Adhesions in and constrictions of the cervical canal may more or less completely occlude it after the termination of menstrual life. Apparently this condition often persists for years, causing no symptoms, but in some cases the lack of drainage from the uterine cavity results in pyometra formation due to infection of postmenopausal secretion of the endocervical or endometrial glands. When the intra-uterine pressure reaches a certain point the adhesions rupture and there is a vaginal discharge of blood tinged purulent material. The adhesions may form again and the discharge stop, only to reappear when the pus in the uterus increases the pressure to a sufficient degree to rupture them.

In 4.4 per cent of our cases nothing was found to explain the bleeding other than fibroids. Since fibroids are present so commonly after the mid-thirties the question is naturally raised as to whether those found after the menopause are merely incidental findings or whether they are the cause of the bleeding. In our series fibroids were found in the uterus in many instances in which there was another obvious cause of bleeding. Those, we regarded as incidental findings and we will not consider them here. In about a third of the cases in which fibroids were the apparent cause of bleeding, sarcomatous change had taken place in them. The breaking down of tissue incident to this discharge obviously was responsible for the bleeding. In most of the other cases the myomata were of the submucous type projecting into the uterine cavity. The question arises whether these occupied the submucous position before the menopause or whether they progressed toward the cavity later. From examining the specimens it would seem that in many cases they scarcely could have been in their submucous position without having caused profuse bleeding before the menopause which would have necessitated their removal. In many of the cases several years had elapsed since the menopause without bleeding. It would seem reasonable, then, to assume that an intramural fibroid which is present before the menopause may work toward the uterine cavity after the menopause and bleed. From a clinical standpoint the important thing to bear in mind is that when a woman with postmenopausal bleeding presents herself and fibroids are found, one has no right to consider the fibroids the cause of the bleeding and defer a complete investigation. More often than not, the fibroids will be found to be incidental and the investigation will reveal some other lesion as the source of the blood.

The relation of ovarian tumors to postmenopausal bleeding is an important one. In about one-fourth of our ovarian tumors

which occurred after the menopause there was uterine bleeding. Often bleeding is the first symptom which calls the patient's attention to the fact that all is not well with her pelvic organs. Ovarian tumors of various types may be present. The appearance of blood from the uterus in the presence of an ovarian tumor is no indication of the histologic nature of the ovarian growth. About half of the ovarian tumors associated with uterine bleeding were benign and approximately half were malignant. The manner in which these ovarian growths cause bleeding is not always apparent. With malignant tumors extension of the growth to the uterine cavity, directly or via the tubes, frequently explains the bleeding. In benign growths, however, such as cystadenomas, no such explanation is possible and there is no evidence that these tumors have a hormonal effect. In the relatively rare granulosal cell tumors there is every reason to believe that the estrogenic hormone is produced in them. This belief is based upon several bits of evidence: the increase in size of the postmenopausal uterus to that of a woman in active menstrual life; the almost constant presence of endometrial hyperplasia in the endometrium; the occasional evidence of breast hypertrophy; and the production of estrus in spayed laboratory animals in which such tumor tissue has been implanted.

In a small group of women with bleeding after the menopause no pathologic lesion can be demonstrated in spite of careful and thorough investigation. It has been suggested by some that hypertension and arteriosclerosis may be responsible for the rupture of endometrial vessels with resultant bleeding. The term uterine apoplexy has been suggested as descriptive of these cases. The idea is attractive, but there are no convincing pathologic data to substantiate it. In our series, in the group with bleeding not explained on an obvious organic basis, the average blood pressure was not abnormally high and we are inclined to be skeptical concerning the hypertension-arteriosclerosis theory.

After considering the pathologic lesions which may cause postmenopausal bleeding it becomes apparent that a knowledge of pathology is the bedrock upon which good gynecology is practiced. The procedures required for a pathologic diagnosis are usually obviously indicated. Each case requires a careful bimanual examination and an equally careful inspection of the vaginal and cervical mucosa through a speculum with adequate illumination. If these procedures do not clearly demonstrate the source of the bleeding a diagnostic curettage and often a cervical biopsy must be done. When this is carried out very careful bimanual palpation of the ovaries should be done under anesthesia. If no lesion has been found adequately to explain the bleeding after these procedures, the patient should not be lost sight of but should return at frequent intervals for reëxamination. If subsequent examination shows evidence of ovarian enlargement a laparotomy is indicated. If the bleeding persists after curettage and the cause has not been satisfactorily demonstrated a laparotomy is indicated, providing the physical condition of the patient is satisfactory. In some instances in which this has been done, ovarian neoplasms too small to be detected bimanually have been found to be the cause of the bleeding.

SUMMARY

A clinical and pathologic study of bleeding after the menopause shows that in more than half the patients the cause of the bleeding is malignancy of the generative tract. This being a proved fact, the logical deduction is that a complete investigation of each case is imperative. In many cases this includes an examination of biopsied tissue by a competent gynecologic pathologist. There are, it is true, many benign causes of postmenopausal bleeding, most of which are easily cured, but pathologic studies indicate that the only safe assumption is that malignancy is responsible for the bleeding until unequivocally proved otherwise.

OFFICE TREATMENT OF THE PATHOLOGIC CERVIX*

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NOT so long ago, effective treatment of the pathologic cervix usually meant hospitalization and surgery. Today we can effect cures in the majority of cases with greater efficiency by treatment in the office, without crippling the cervix, and with minimal discomfort and expense to the patient.

This paper will limit itself to the office treatment of nonspecific infections and benign lesions of the cervix. The lesions to be considered are: erosions; endocervicitis; lacerations with eversion and/or erosion; cysts; polyps; strictures; stenoses; leucoplakia; endometriosis; varicosities; "strawberry cervix." The anatomy, physiology, and pathology will be reviewed briefly in order to understand the treatment of these conditions more clearly.

The cervix is the lowermost portion of the uterus, extending from the external os to the internal os. It differs from the body of the uterus both in its anatomy and physiology, although it is developed from the same portion of the Müllerian duct.

The cervix may be divided into the infravaginal portion (portio vaginalis) which projects into the vagina, and the supravaginal portion (portio supravaginalis) which lies in the pelvic cavity, and is supported and encircled by that part of the connective tissue which forms the parametrium. Posteriorly this cellular tissue is part of the uterosacral ligaments, while anteriorly it extends along the less marked uterovesical ligaments. In the lateral parametric cellular tissue lie the uterine arteries and ureters within 2 cm. of the cervix. The parametrium also contains a rich network of lymphatic vessels which drain the cervix and furnish an easy road for the upward spread of infection.

The cervical canal is fusiform in shape, with an average length of 3 cm. (Fig. 1.) Along the midline of the anterior and posterior walls there is a longitudinal ridge from which a large number of oblique folds are given off (plicae palmatae) which by their inclination favor drainage downwards. The mucosa consists of a large number of compound racemose glands, more numerous towards the external os where they are branching and covered by high cylindrical goblet-cell type epithelium. Towards the internal os the glands are fewer, less branching, and the epithelium is low columnar, the nuclei are basal, the cytoplasm clear, and there is a basement membrane. These glands produce an abundant secretion of alkaline mucus, pH 7 to 7.5 which is clear, viscid, colorless, and empties through small ducts into the cervical canal. The epithelium lining the canal is continuous with the epithelium of all the glands which lie in the stroma. Due to this arrangement of rugae and numerous branching glands, the secretory area of the cervix is enormously increased, with a minimum of exposed surface, making the mucosa a forest of crypts, tunnels, and recesses. This epithelium partakes only to a slight degree in the cyclical changes so characteristic of the uterine epithelium, but it is not shed with the menses and therefore does not enjoy the advantage of being cast off and renewed.

At the proximal end of the cervical canal is the internal os where there is a sharp transition between the cervical and uterine epithelia. At the distal end is the external os, where normally the glandular epithelium ceases and stratified squamous epithelium begins, covering the portio vaginalis. The external os is encircled by

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the anterior and posterior lips, and is normally in close contact with the posterior vaginal wall.

Erosion. This is the most common lesion. It is seen as a bright red circular area of varying size, immediately surrounding the external os. It may be smooth or softly irregular to the touch, and may bleed easily on sponging. It is classified as simple, papillary or follicular depending upon the number and degree of the downgrowth of the glandular element. This differentiation does not influence the treatment, and need not be discussed now. Although erosion is frequently referred to as "ulcer," it is actually covered by a single layer of columnar epithelium.

From the clinical standpoint, cervicitis may be divided into two groups: in one group, disturbance of physiology is the etiologic factor; in the other, which comprises most of the cases, the cause is infection.

In the first group, erosion is the only lesion, and the endocervical mucosa is normal in structure. The glands may function normally, or there may be excessive secretion. These erosions may be congenital or acquired. In a series of 500 cases of cervicitis in private practice Holden[1] found that one out of five occurred in unmarried women, eighty-five of these hundred patients having hymens so small and sharp edged as to be classed as verifiable virgins. (Fig. 2E.)

Wollner[2] has done some interesting experimental work showing that estrin has a stimulating effect on the growth of the columnar epithelium and progestin stimulates the proliferation of the squamous epithelium, and the balance between these hormones has a direct bearing on the columnar-squamous cell proportions of the cervical epithelium.

In the group where infection is the cause, a small number are due to endocervicitis resulting from vulvovaginitis in childhood. In many of these, the cervix was infected by the hematogenous route as a complication of the exanthemata, particularly scarlet fever.[3] Some of these childhood infections are gonorrheal in origin.

The greatest proportion of cases is found

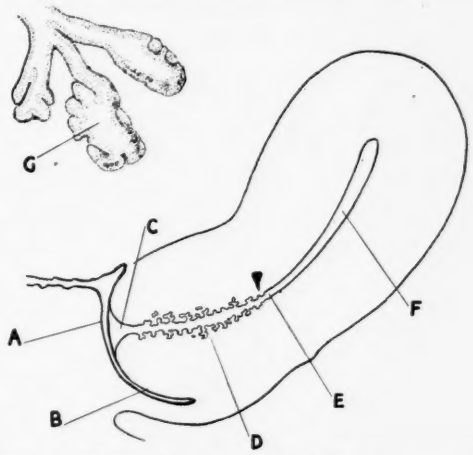


Fig. 1. Schematic drawing of the anatomy of the cervix. A, mucosa of vaginal vault in direct contact with B and C, external os surrounded by both lips. D, epithelium of cervical canal with its branching racemose glands. E, internal os. F, uterine cavity. G, single gland of cervical canal showing branching and crypts.

in parous women, in 50 to 80 per cent of whom erosions are found following delivery. In this group, the predominant organisms are staphylococcus, streptococcus, and *B. coli*. The gonococcus is responsible for another large percentage of cases, with the endocervical mucosa as the primary site for this type of infection. Secondary invaders often contribute considerably to the pathology, and may remain long after the gonococcus has disappeared. There may or may not be involvement of the portio as well. In private practice, the gonococcus is much less frequently seen as a cause of cervicitis than the nonspecific organisms.

Because of its anatomy, when the endocervical tissue becomes infected, the bacteria lodge in the crypts and lacunae of the racemose glands, causing a glandular proliferation, exudation, edema, vascular engorgement, polymorphonuclear, round and plasma cell infiltration. The hyperplasia and hypertrophy of the glands are accompanied by hyperfunction, resulting in an excessive amount of mucopurulent alkaline discharge.

The portio vaginalis with its stratified squamous epithelium accustomed to the acid medium of the vagina with its pH 4 or 4.5 thus lies in a pool of mucopus with an alkaline reaction of pH 6 to 7.5. In addition, the subepithelial area becomes heavily invaded by bacteria and cellular infiltration, often with small subepithelial hemorrhages. The squamous epithelium becomes raised, macerated, and in a short time the area surrounding the external os becomes denuded, forming a true erosion.[4] This lasts only a short time, for nature will make every effort to re-epithelialize. The columnar epithelium of the endocervix which can live in this alkaline medium, grows downward and over the denuded part of the portio, forming a bright red area covered by a single layer of columnar epithelium, which is the erosion as we see it clinically. (Fig. 2A.) When the infection is improved or cured so that the endocervical secretion is normal in amount and character, the external os is again in an acid medium, giving the stratified squamous epithelium of the portio the upper hand. In the reparative process, the squamous epithelium displaces the glandular epithelium until the eroded area is entirely epithelialized with squamous epithelium and the erosion is healed.

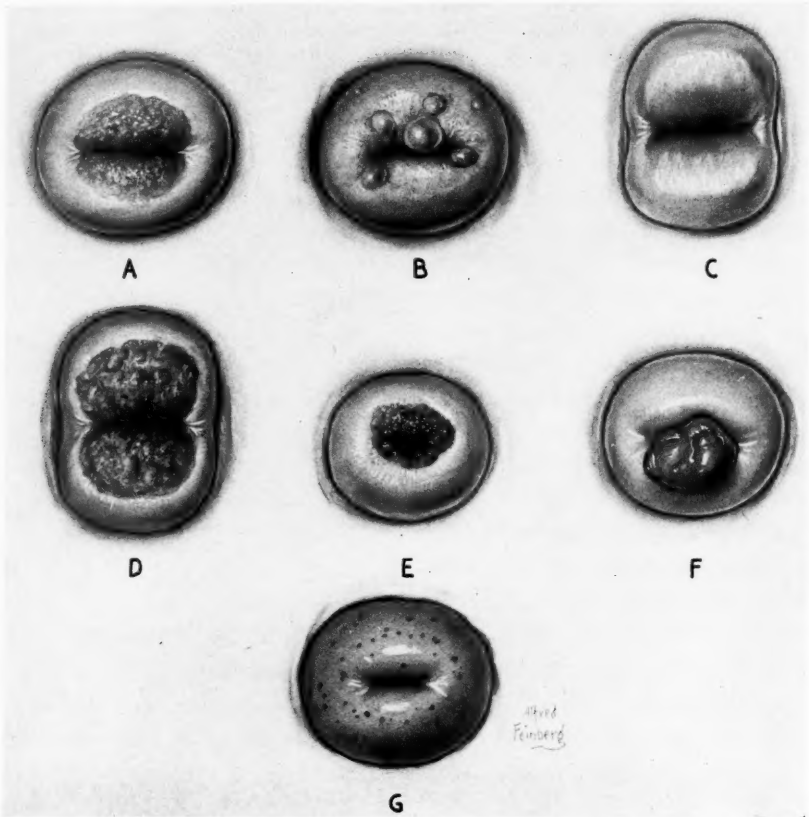


FIG. 2. Lesions of the cervix. A, erosion. B, Nabothian cysts. C, bilateral laceration healed. D, bilateral laceration with eversion and erosion. E, erosion in a virginal cervix. F, polyp. G, strawberry cervix.

Roblee[5] thinks that the vaginal pH is the primary factor in inducing erosions. In his series, cervices subjected to a pH of 6.5 to 7.5 showed some columnar proliferation and an acute cervicitis. When the medium was then changed and maintained at pH 4 to 4.5, these same cervices showed some squamous cell epithelialization with a retreat of the columnar epithelium.

Nabothian Cyst. In this process of destruction and repair, the duct of many a cervical gland becomes occluded so that its secretion has no exit. The accumulation of

this secretion forms a cyst which on the vaginal surface looks like a translucent pearly area. Rarely this will contain pus instead of clear mucus, forming a Nabothian abscess. Often these cysts are not visible, as they may occur deep in the portio or high in the canal.[6] When many of these cysts are found, the cervix is described as cystic. (Fig. 2B.)

Lacerations of the cervix are due to trauma, usually during labor, occasionally if too forceful a dilatation is done preceding curettage. The laceration may be unilateral, bilateral, or stellate. It may be small or large enough to extend outward into the parametrium. Lacerations usually heal spontaneously. A healed laceration is of no danger and needs no treatment. (Fig. 2C.) It requires attention only when complicated by chronic infection, erosion, or ectropion. Eversion or ectropion occurs in conjunction with a bilateral cervical laceration which allows the endocervical tissue to pout out into the vagina. (Fig. 2D.)

Polyps are caused by a hyperplasia of the endocervical mucosa. They are usually single, but may be multiple, and are pedunculated. They are usually accompanied by a low grade endocervicitis, and are easily seen and felt as soon as they extend to or beyond the external os. (Fig. 2F.)

Strictures and Stenoses. These lesions are frequently overlooked, and are usually a result of endocervicitis or of the treatment for this condition. Occasionally, they follow a poorly executed surgical repair or a very traumatic obstetrical delivery. Intrauterine radium therapy may lead to subsequent stenosis. Senile atrophy occasionally may cause stricture, and rarely complete occlusion. When these lesions follow cauterization, conization, or coagulation of the cervical canal, it is often due to the fact that the operator was not sufficiently familiar with the technique.

Leucoplakia is rare. It is a circumscribed irregularly shaped patch of white thickened mucosa, and is of importance because some believe it has malignant potentialities.[7]

Endometriosis is very rare and is seen as small endometrial transplants on the portio vaginalis and in the vaginal mucosa of the vault. These transplants are ¼ to 1 cm. in diameter, and look like dark blue Nabothian cysts.

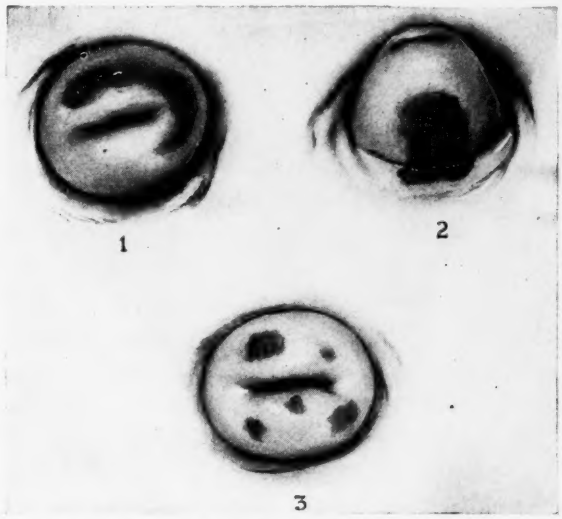


Fig. 3. Various types of superficial ulcerations seen in some cases of trichomonas vaginalis vaginitis. (From Kleegman, in *Surg., Gynec. & Obst.*, 51:552, 1930.)

"*Strawberry Cervix.*" This term is applied when the epithelium of the portio is reddened and has numerous spots of a deeper red, so that the cervix looks like a strawberry. (Fig. 2G.) It is part of any acute vaginitis. In addition, superficial ulcers of the portio occasionally occur in acute trichomonas vaginitis. (Fig. 3.) It is not necessary to treat the cervix apart from the vaginitis, and the condition is mentioned here only to complete the picture.

Incidence. A pathologic cervix is the most prevalent of all gynecologic disorders and the anatomy of the canal almost precludes any spontaneous cure. Polak[8] stated that 85 per cent of all women had cervicitis. Fulkerson[9] in a review of 6,483 gynecologic records found a diagnosis of cervicitis made in 33.16 per cent; 80 per cent of these had been pregnant and 20 per cent had never been pregnant. We have found an incidence of cervicitis in 50 per cent of our private patients, 80 per cent of whom had been pregnant.

Symptoms. Leucorrhea is the most common and frequently the only symptom, occurring in 80 per cent of all cases. Usually it does not cause itching or irritation. There are no symptoms in 20 per cent of cases. Additional symptoms commonly present are backache, sense of weight in the pelvis, menorrhagia and metrorrhagia, dysmenorrhea and occasionally dysuria. Sterility[10] will follow when the purulent cervical secretion forms a mechanical barrier which the sperm cannot penetrate. This latter assumption should always be checked by means of the Hühner test.[11] When the infection extends in the cellular tissue along the uterosacral ligaments, making them thickened and tender, then backache and dyspareunia are the two common symptoms. Cervicitis is a potential focus of infection. In a small series Moench[12] produced acute arthritis in animals with streptococci which she isolated from cases of cervicitis. An occasional case of arthritis will be cured only after the cervical infection has been cured or removed.

Polyps and endometriosis of the portio will often cause pre- and postmenstrual and postcoital spotting. Varicosities, if marked, cause a sense of weight in the pelvis. A ruptured varix will cause bleeding. Leucoplakia causes no symptoms.

Stenosis will give a history of dull premenstrual pain, severe comenstrual pain at the height of the flow, with a prolongation of the period. If the stenosis has resulted from cervical treatment, the patient will date her symptoms since the procedure. Amenorrhea accompanied by considerable abdominal pain means complete obstruction. The sudden appearance of a profuse purulent discharge after the menopause is often due to a pyometra caused by cervical stricture.[13]

Differential Diagnosis. Erosions must be differentiated from carcinoma. In early cases this is very difficult, if not impossible. Schiller's[14] test consists of painting the eroded cervix with fresh Gram's iodine solution. This test is based upon the fact that the vaginal cells are rich in glycogen, whereas carcinoma cells contain little or no glycogen. Benign lesions take a mahogany brown stain, whereas malignant tissue does not take the stain. This test is useful only as an aid, and cannot be leaned upon too heavily. Examination with the colposcope[15] is also only an aid. Nothing can take the place of expertly trained senses, aided by adequate exposure, good light and careful inspection in order not to overlook possible suspicious lesions. Biopsies must be taken of all suspicious areas. These should include some of the surrounding normal tissue and can be taken either with a biopsy punch or by the use of a thin wire loop electrode attached to a fast cutting current. After using the biopsy punch, it is well to sear the raw surface with the cautery. When a cervical erosion does not respond to the treatment to be described, always be suspicious of carcinoma and take a biopsy. It requires an expert pathologist to make a diagnosis of a biopsy specimen, especially in these early cases, otherwise a malignant lesion will be overlooked, or a benign lesion will be erroneously diagnosed as malignant.

Painless, bright red bleeding late in pregnancy may be due to a ruptured varix, an extensive erosion, or to a polyp. Therefore, with scant or moderate amount of bleeding, a diagnosis of placenta previa should not be made without adequate inspection of the cervix.

Syphilis of the cervix is difficult to diagnose. A chancre in its early stage may be easily mistaken for an erosion, since it is usually centrally located involving the external os.[16] When eccentric, the posterior lip is involved more often than the anterior lip. A little later, the chancre looks like a funnel shaped ulcer with a grayish membrane at its base, which when removed, bleeds very little and has little discharge. It is usually an accidental finding because it is symptomless and fleeting. Secondary lesions of the cervix have the same characteristics as secondaries anywhere else. Accompanying these lesions, there is an

enlargement of the sacral, lumbar, and hypogastric glands, and in some cases these can be palpated as discrete tender nodules posteriorly and laterally behind the broad ligaments. The diagnosis can be substantiated only by the positive dark field examination. Local treatment is useless, and valuable time may be lost if this condition is not borne in mind.

Gumma and tuberculosis of the cervix are very rare. They are usually mistaken for carcinoma, and the diagnosis is made only on examination of a biopsy specimen.

Prophylactic Treatment. Artificial dilatation of the cervix, or forcing a fetus through a rigid undilated cervix either by traction or injudicious use of pituitrin may cause extensive lacerations. When the surroundings are aseptic and the patient is in good condition De Lee[17] advocates inspection of the cervix under good light and adequate exposure immediately after delivery, and repair of all cervical lacerations. Hasty and traumatic cervical dilatation preceding a curettage may also cause laceration.

Reduction of gonorrhea by education and prophylaxis would reduce cervical infection tremendously.

Discovering the cervicitis is an important step in the prophylaxis. With increasing education in preventive medicine, more and more women are coming to the physician for yearly physical examination. The pelvic organs are usually excluded from this check-up by a large percentage of physicians. No woman has had an adequate survey without a gynecologic examination, including careful inspection of the cervix. With the proper mental attitude of doctor and patient, and with suitable instruments and the necessary experience this could readily be done even through the undilated hymen in almost all cases. I do not advise routine vaginal examinations of the young girl, but when dealing with the mature woman who comes to see "if she's all right," there is no excuse for ignoring such an important part of her body as her generative organs. In women who have had a supracervical hysterectomy, it is equally important to examine and carefully inspect the cervical stump at regular intervals.

Adequate postpartum care is another important measure. Even in this group the cervix is often overlooked. Despite good obstetric care, labor is still one of the important etiologic factors in initiating cervical pathology. Of all women examined in the postnatal period, 50 to 80 per cent require some cervical treatment.[18] The present custom of discharging the woman after one examination six weeks postpartum is inadequate care. In many instances a cervix may look fairly healthy at this time and the uterus may be in good anteversion, yet when the same patient is seen three to four months postpartum the cervix may present an erosion and the uterus may be found in retroversion. Patients should be seen six weeks, two, four, and six months postpartum in order to make sure the cervix and uterus are in good condition and position.

All authorities agree that carcinoma does not occur in a healthy cervix, and although the word "precancerous" is looked upon with disfavor, pathologists nevertheless consider cervicitis a precancerous lesion. All large studies confirm the view that the most important and effective means of treating cancer of the cervix is to prevent its occurrence by curing the lesions of the cervix while they are benign. Dickinson, Holden[19] and others have not seen carcinoma arise in any case of cervicitis that they have treated. In this country, 16,280 women died of carcinoma of the uterus in 1936, 80 per cent being of cervical origin. These deaths could be reduced greatly by proper care of the cervix. In order to give appropriate treatment, a complete physical examination must include careful inspection of the cervix.

TREATMENT

Chemical Treatment. Topical application of large numbers of various chemicals has been and still is for the majority of practitioners the method of choice in

treating cervical pathology. This should not be so, for in most instances, the chemical treatment is inefficient and unduly prolonged. Referring back to the anatomy of the endocervical mucosa, one can realize how futile it is to try to cure a chronic infection of these glands with topical applications or douches. There are two classes of exceptions to this statement. In cases of acute erosions, where thermal or electrical measures are contraindicated, painting the erosion with a chemical has its place. In other cases where the infection is only superficial and can be quickly cured by a surface attack, topical application of a chemical may be indicated. The favorite drugs in use are various silver preparations, mercurochrome, aniline dyes and tincture of iodine.

For the past two years in the Bellevue Hospital clinic and in private practice we have treated cervicitis with a product called negatol. In our experience, we have found this superior to the foregoing chemicals mentioned. Negatol is an aqueous solution of the colloidal products formed by reacting cresol sulfonic acid with formaldehyde. It comes as a liquid, powder, or suppository.* In a preliminary report of a series of ninety-seven cases of cervical erosions treated with topical applications of 100 per cent negatol solution twice weekly, 69 per cent were cured, 24 per cent improved and 7 per cent unimproved. The average number of treatments was seven, over an average period of time of fifty days. In 20 per cent of the cured cases the erosions were graded as of severe degree.[20]

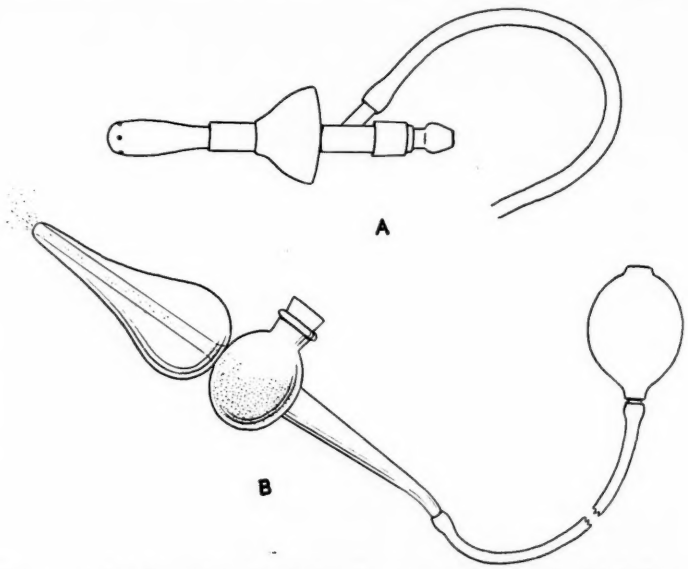


Fig. 4. A, douche point. Conical collar is movable, and with inflow and outflow circuit vagina can be distended, making douche more effective. B, powder blower. Vaginal outlet can be closed so that with pressure the vagina is distended, allowing the mucosa and especially the vault to become thoroughly powdered.

However, negatol is not so effective as the electrical methods to be discussed, and has a place only when these more efficient measures are contraindicated.

Caustics. Local applications of caustics, such as chromic acid crystals[21] and caustic potash crayon[22] likewise are not so effective. They result in a higher percentage of cervical stenoses, and have been discarded by us.

Powders. Based on his work with vaginal acid-alkali relationship to cervical erosions, Roblee[5] has cured superficial erosions by maintaining the vaginal acidity continuously between pH 4 and 4.5. This he does by having the patient insert

* Supplied to us for experimental purposes through the courtesy of Eli Lilly Co.

nightly a gelatine capsule containing 12 c.c. of a powder mixture of B lactose 80 per cent and boric acid 20 per cent. The pH of the vaginal secretion can be tested with sufficient accuracy by using fresh nitrazine paper as an indicator.[23] Vinegar douches (2 ounces to 2 quarts) are taken only after coitus and during the menstrual period, the instillations of the powder being continued after such douching. A more efficient means of powdering the entire vaginal mucosa, especially the region of the vault, is to insufflate the powder by means of a vaginal powder blower. (Fig. 4.) Here again, this treatment is more tedious, and often less effective than the electrical methods. Roblee states that simple erosions will respond to this treatment, but that it is insufficient to cure papillary or follicular erosion. The value of the method lies chiefly in that the patient can carry on the treatment herself; it is also helpful where electrical methods of treatment are contraindicated.

Injection of various chemicals into the cervix,[24,25,26] medicinal pastes[27] and ionization treatment[28] whereby metal ions are forced into the cervical tissues have been recommended by various isolated workers. We have no personal experience with them.

Electrosurgical Methods. Thermal Treatment. From the earliest antiquity, heat in one form or another has been held in high esteem as a therapeutic agent. Nearly every type of lesion or wound has been treated with the hot iron. Hippocrates used fire for healing. In 1811 Percy recommended treating the ulcerated cervix with a glowing iron, and this was carried out in 1843 by De Lambelle. In 1906, Hunner[29] used the Paquelin cautery in the treatment of endocervicitis. In 1911, Dickinson[30] began the treatment of cervicitis with the fine wire nasal tip cautery, and this method has proved to be the safest and most effective for the largest percentage of cervical lesions.

We have discarded the use of the heavy duty electrical cautery, the Paquelin cautery, and the Post cautery, as the heat is not sufficiently restricted, and too often extensive scar tissue with subsequent stenosis is the result.

Cauterization of Cervical Erosions, Nabothian Cysts, Endocervicitis, Polyps, Endometrial Transplants, Cervical Varicosities by the Nasal Tip Cautery Points. This form of therapy has been the greatest advance in the treatment of cervical pathology, since the method is technically the simplest and most foolproof. The apparatus required is the least expensive of any of the electrical methods, few treatments are necessary, and the results are excellent. The necessary experience can be easily acquired by any physician, and the possibility of complications is by far the least of any method of treatment.

However, damage can be done unless the proper technique is employed. There are likewise contraindications which pertain to all the electrical methods to be described.

Contraindications. Cauterization should not be done on an acutely infected cervix, nor in the presence of acute or subacute pelvic pathology. If these contraindications are not heeded, serious and extensive pelvic infection may flare up as a result, occasionally resulting in death. This is especially true in the presence of an acute streptococcus infection. We do not cauterize when spreads are positive for gonococci. However, Goldblatt[31] treated 2,627 cases of gonorrheal endocervicitis by means of electrocoagulation and/or conization, twenty of whom were from one to nine months pregnant. He claims that the acuteness of the infection was no contraindication and did not affect the healing. The twenty pregnant patients all went to full term and had uneventful deliveries.

Technique. The apparatus needed consists of rheostat, a handle, and an electrode. The electrode should have shanks 6 to 8 inches long with tips of various shapes made of platinum fine wire. (Fig. 5.)

Good exposure of the cervix and good light are essential. It is not necessary to use a tenaculum.

To cauterize an erosion, no anesthesia is required, even on the nervous patient, as the portio is insensitive. Cleanse the cervix with peroxide or tincture of green soap. Dry. With the blade tip heated to a bright red, cauterize the posterior lip first, starting from the external os to the outer margin of erosion. The strokes should be slow, even, about 2 to 4 mm. deep and 0.5 to 1 cm. apart. The same procedure is carried out on the anterior lip, starting from the outer margin of the erosion and extending down to the external os, but stopping short of it so that no two cauterized stripes on apposed lips are left in direct contiguity with each other. This will avoid possibility of stricture. (Fig. 6.)

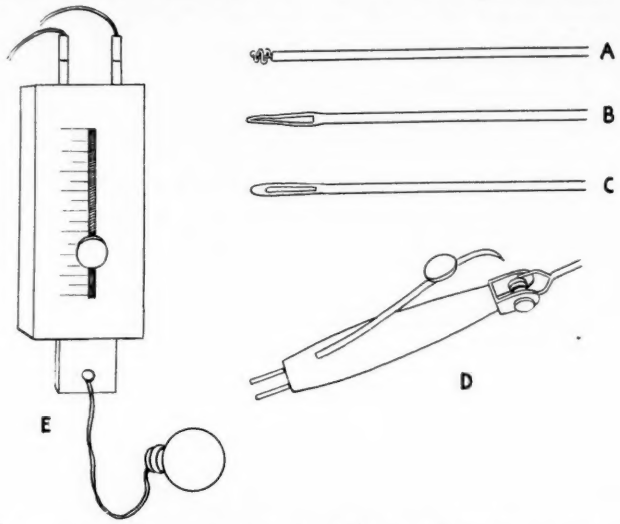


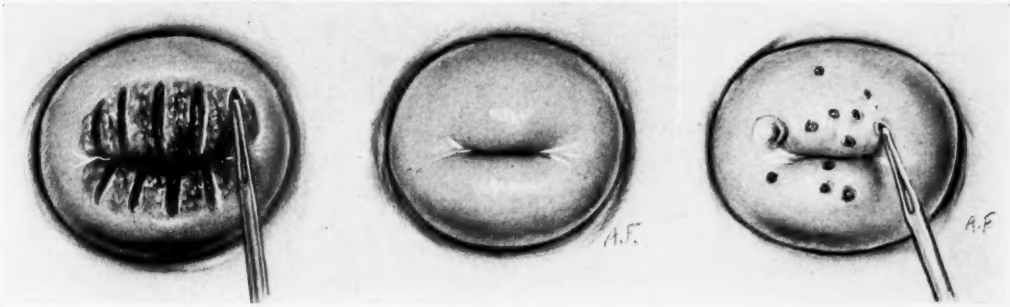
Fig. 5. Armamentarium for nasal tip cauterization. A, B, C, different types of cautery tips. Only the terminal tip heats up, the handle remaining cold, so that the heat is restricted to the point of application. A, corkscrew for endocervical cauterization. B, pointed tip for Nabothian cysts, varicosities, and endometrial transplants. This may also be used for erosions. C, blade tip for erosions and removal of polyps. D, handle. E, rheostat.

Bleeding. In gauging the heat of the tip by its color, the light of the surroundings must be taken into account. In a brightly lighted room a bright red tip may look dull red. Therefore the heat of the tip should be estimated in dim light (under the table is usually an accessible place). The patient should not see the cautery point. Too much heat will burn out the tip, or may cause bleeding. The cervix should be left thoroughly dry before the speculum is withdrawn. To stop oozing, the heat is reduced to so low a point that the tip barely glows, then the tip is held directly against the oozing point until the latter is seared and thoroughly dry. If any point is allowed to continue to ooze, it may give rise to troublesome bleeding subsequently.

Very rarely, oozing may begin about seven or ten days after cauterization when the slough separates. All oozing points can be stopped promptly with the above procedure. We have never found bleeding a problem with this type of cauterization.

If the canal needs to be cauterized, it should be well cleansed and dried first. The most effective means of getting rid of the thick cervical secretion is by the use of caroid powder. A cotton applicator dipped in this powder is rotated in the canal, the mucus is digested by the powder, and the canal is cleansed of all secretion. The canal is sensitive, and good anesthesia is obtained by inserting one or more cotton applicators saturated with 10 per cent novocaine solution, to remain for ten minutes. This at the same time will stop all oozing which the caroid powder may have started.

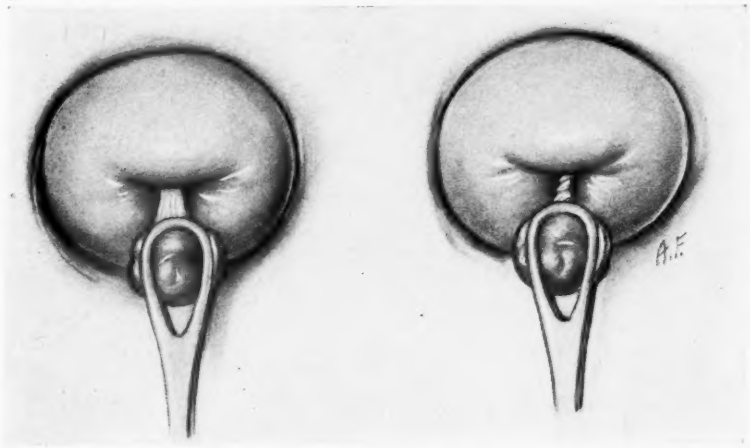
For this work either a straight or corkscrew electrode is chosen. Experience will guide the choice. With a widely open surfaces are left in direct apposition. This means that only one-half of the canal surface is cauterized at the same sitting,



A FIG. 6. B FIG. 7.

FIG. 6. A, cauterizaton of an erosion with the nasal tip cautery. The posterior lip has been cauterized and the last stroke is being made on the anterior lip. Stripes on both lips are made from above downward. Note that the stripes on the anterior lip do not extend as far into the external os as those of the posterior lip, so that raw areas of the lips will not come in apposition. B, end result after a total of four visits. Cauterization was done twice.

FIG. 7. Cauterization of Nabothian cysts with straight tip. The cyst wall must be destroyed.



A B

FIG. 8. A, polyp grasped and traction applied. In actual practice, the pedicle is grasped much higher, as close to the base as possible. B, combined traction and rotation until polyp is twisted off, after which the base is cauterized.

external os, the straight tip may be better, while with a small external os, the spiral tip is usually preferable. With a small external or tight internal os, the canal should be gently and gradually dilated up to the size No. 10 to 12 with the Hegar's dilators. The degree of heat is chosen, the tip put in cold and then the heat turned on. The heat is again turned off before the tip is withdrawn. This will prevent undue cauterization of the external os. The cauterization is done with linear strokes from above downward, with care, especially in the region of the internal os, that no raw the other half being done when the first has healed. If these simple precautions are taken, there will be no resultant stricture or stenosis as a result of this type of cauterization. (Fig. 9C.) Cauterization is best done four to six days after menstruation.

Undercauterize rather than overcauterize. All contraindications to cauterization should be heeded.

Nabothian Cysts, Endometrial Transplants, Cervical Varicosities. For the cysts, a sharp pointed electrode is used, the current turned on, and the tip plunged into the cyst. This may have to be done several

times in order to get rid of the collected mucus, after which the cyst wall is cauterized until completely destroyed. (Fig. 7.)

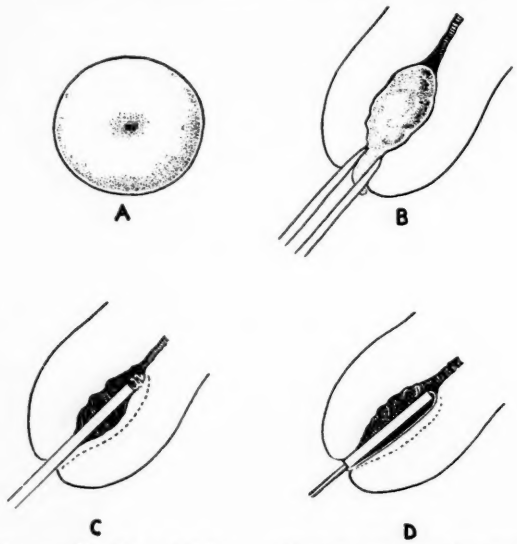


Fig. 9. Endocervicitis. A, there is no erosion and the cervix looks apparently normal. B, on introducing a uterine dressing forceps through the external os, and separating the blades, it is seen that there is a thick mucopurulent discharge filling the canal. This is the type of cervicitis that causes sterility. C, the canal has been cleansed, dried, and anesthetized. The corkscrew tip is inserted to the internal os, the current turned on, and the tip slowly drawn downwards as outlined, cauterizing the indicated strip of mucosa. The current is turned off before the tip is removed so as not to burn the external os. Three such stripes are burned parallel to each other over one-half the circumference of the canal. The other half is similarly cauterized six weeks later. D, Hyam's conization. The canal is similarly prepared, but the degree of anesthesia is greater. The current is turned on, the electrode introduced up to the internal os, then a complete circle made as the wire cuts through the mucosa of the canal, coring out the endocervical mucosa.

Many of these cysts are invisible, occurring higher up in the cervical canal, and are found accidently while cauterizing the canal.[6]

Endometrial transplants and varicosities in the cervix are cauterized until completely destroyed, in a manner similar to that described for the Nabothian cysts. For varicosities, a dull red heat should be used.

Polyps. If the pedicle is thin, as it usually is, grasp the pedicle close to its source with a sponge stick or curved clamp, and with traction, rotate the polyp on its pedicle, twisting it off. This is a simple procedure, and usually there is no bleeding. (Fig. 8.) The site of origin is then cauterized

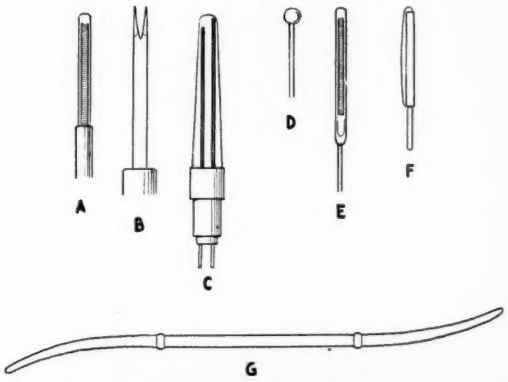


Fig. 10. Armamentarium for electrocoagulation and conization. A, Cherry electrode. There is a similar strip on the other side of the electrode so that opposite sides of the canal become coagulated at the same time. B, bipolar tip for cysts and erosions. C, Ende electrode. Here only the tissue between the two strips is coagulated, making it possible to control the area done at one sitting. D, ball tip electrode used by Barrett for electrocoagulation of erosions. E, tip used for coagulation of canal. Here there is only one strip as shown, so that the area treated can be controlled. F, Hyam's tip for conization of canal. These come in several lengths and shapes to fit various types of canals. G, Hegar's dilator for dilatation of the cervical canal.

with the straight or corkscrew nasal tip cautery. If the pedicle is thick, it is grasped, pulled downward, and severed at its base by slowly cauterizing with a dull heat, using the straight electrode. Care is taken to preserve the polyp during removal, as all polyps are routinely subjected to microscopic examination to avoid overlooking an occasional case of malignancy.

Erosions may be cauterized and polyps removed during pregnancy. Cervicitis increases puerperal morbidity,[32] and may safely be cleared up in the antepartum period. Since the majority of spontaneous abortions occur in the first trimester of pregnancy, it is wise to postpone this therapy until after the third month and thereby avoid the undeserved blame of a possible coincidental spontaneous abortion. Because of the greatly increased vascularity of the tissues, a low degree of heat

(cherry red) is used, and we have had no untoward results in any of our pregnant cases.

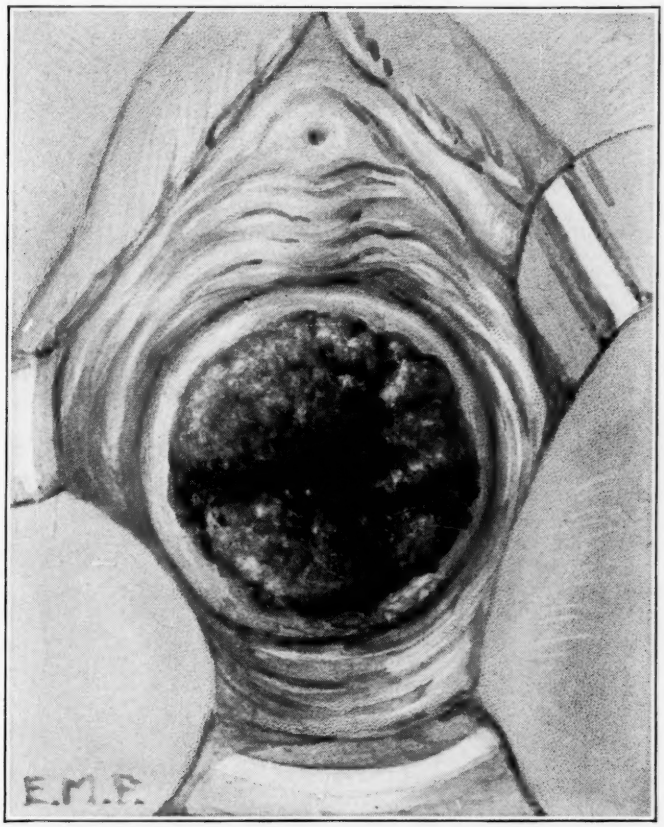


Fig. 11. Primipara eight weeks postpartum; before treatment. Note lacerations and extensive erosion. (From life drawing.) (From Barrett, in *J. A. M. A.*, 103:1516, 1934.)

After-Treatment. The patient is seen two weeks, four weeks, and six or eight weeks after cauterization. Two weeks after cauterization the slough will be cast off, or is ready to be removed, leaving a raw area. This area is cleaned with peroxide or tincture of green soap, dried and a topical application made with 100 per cent negatol solution. This treatment is repeated two weeks later. Six to eight weeks after cauterization healing has taken place. If there are any unhealed areas of the portio or canal, these can now be recauterized.

The patient is warned that following cauterization she will have a profuse discharge, frequently blood tinged, for a period of two weeks, after which it will rapidly subside. Coitus is interdicted for the first two weeks. After the first week, the patient may douche if she wishes to, with some cleansing solution such as 1 ounce of tincture of green soap or 2 ounces of vinegar to 2 quarts of warm water. Many cases are cured with one cauterization, some require two, and only the occasional case will need more. We do not recauterize until at least six weeks and preferably eight weeks after the previous cauterization.

This is the method in use in the Gynecological Clinic at Bellevue Hospital, and is most commonly used in our private practice as well. We have found no method superior to the nasal tip cautery for the cure of erosions. Healing takes place without formation of scar tissue and the area is covered with normal squamous epithelium. In my personal series covering thousands of cases, there have been no complications nor untoward results.

For endocervicitis, there are a small group of cases where electrocoagulation and conization give results superior to the nasal tip cautery, particularly where there is a small external os, with a ballooned out chronically infected endocervical mucosa beyond it. (Fig. 9 A and B.)

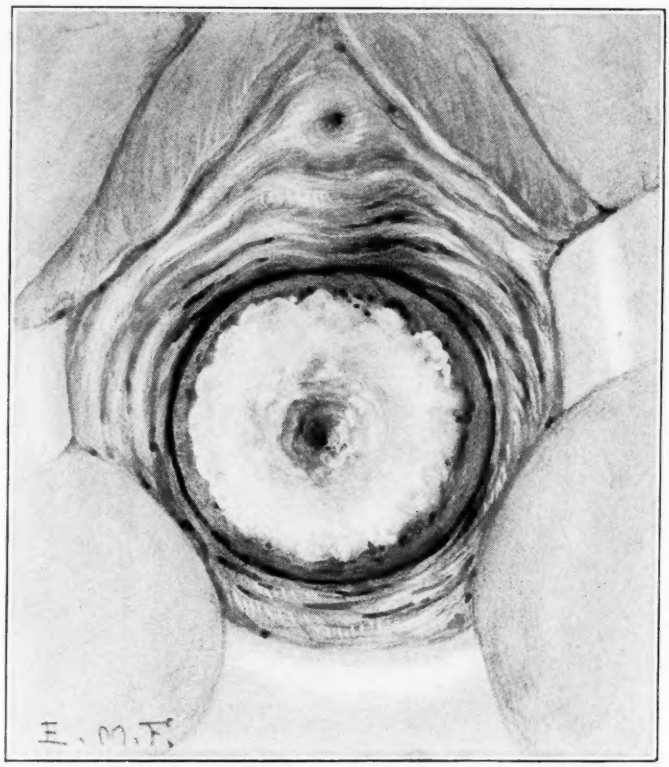


Fig. 12. Immediately after electrocoagulation. Note white coagulum. (From life drawing.) (From Barrett, in *J. A. M. A.*, 103: 1516, 1934.)

Electrocoagulation. For this it is necessary to have a diathermy or radio tube machine and electrodes. Ende[33] devised a good one, and Cherry[34] has a modification of the Ende electrode. One disadvantage of the Cherry electrode is that, because of the placement of the metal strips, raw surfaces are left in apposition and the possibility of subsequent stenosis is increased. After the canal is cleansed, dried and anesthetized as previously described, the electrode is inserted into the canal, pressed against the wall and the current turned on for the required dosage. The handle is gradually rotated until a coagulation of half the canal is obtained, 2 mm. in depth. Ende recommends that a gauze soaked in enzymol be left in the canal for forty-eight hours after this procedure. The other half of the canal is treated eight weeks later. When necessary, treatment may be repeated at eight week intervals. For erosions and cysts, the bipolar electrode is used, and the superficial tissue between the tips coagulated. (Fig. 10.)

For electrocoagulation of cervical erosions and endocervicitis in the late puerperium, Barrett[35] prefers the radio tube machine with ball tip electrode causing electrocoagulation of the eroded area. (Figs. 11, 12 and 13.) Workers using this method have corroborated his excellent results. In a small series of extensive erosions of both lips, I have treated one lip with the nasal tip cautery and the other lip with Barrett's method and have found healing the same in both lips as to time and degree.

Conization. Hyams[36] devised a technique whereby the infected glandular tissue in endocervicitis can be quickly

excised, analogous to the Sturmdorf[37] operation both as to tissue removed and degree of healing obtained. By means of his

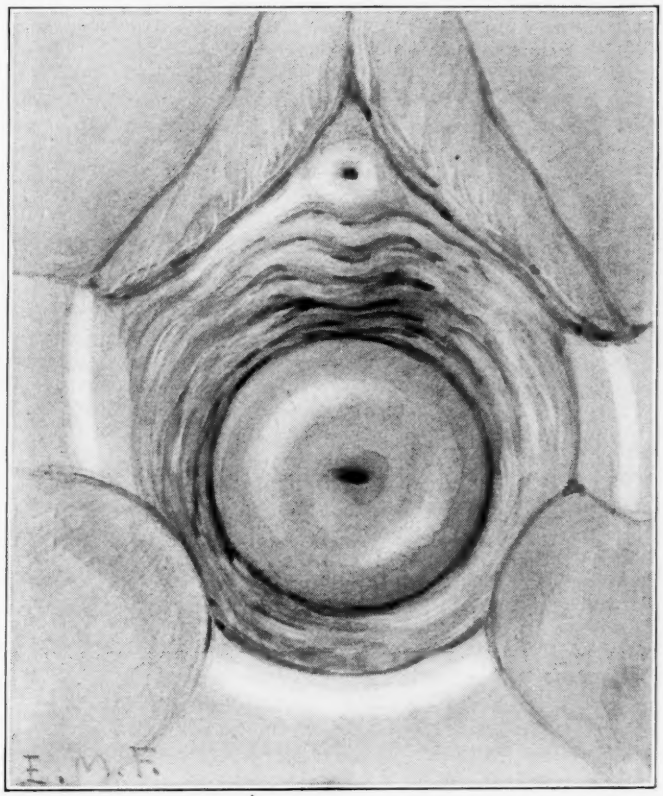


Fig. 13. Six weeks after electrocoagulation. Note normal appearance of cervix. (From life drawing.) (From Barrett, in *J. A. M. A.*, 103: 1516, 1934.)

electrode with a fast cutting current, Hyams cones out the mucous lining of the cervical canal and its glands without injury to the underlying musculature. It is an office procedure and when properly done, as simple for the patient as any of the others.

Armamentarium. The apparatus needed includes a diathermy or radio tube machine which can generate a fast cutting current, an inactive electrode 6 by 6 inches with a sandbag to hold it in place, and special electrodes of varying size and shape with silicon tip and a tungsten wire for cutting. (Fig. 10F.)

Technique. The canal is cleansed and dried. One or more cotton applicators saturated with 35 per cent cocaine solution are placed in the canal for ten minutes, as this method requires a greater degree of anesthesia than the others. This gives excellent anesthesia, even for the nervous patient. In applying cocaine hydrochloride solution to the cervical canal, there have been no reactions even though 35 per cent or 50 per cent solutions are used routinely. The cervical canal is the only orifice where such concentrated solutions of cocaine may be used with impunity. The tip selected depends upon the length and shape of the canal. The inactive electrode is moistened, placed upon the lower abdomen, held there by a sandbag and the patient is directed to make firm pressure on the sandbag, merely to divert her attention. The current is turned on to the proper degree, having just previously been tested on raw meat. With the current on, the silicon's end is passed into the canal to the internal os (Fig. 9D), the spark cutting through the tissue, and the tip is rotated through 360 degrees, coning out the entire epithelium lining the canal. It is helpful to use a bakelite speculum, but if a metal speculum is used,

do not let the tip come in contact with the speculum, as the tip will be destroyed. Hyams packs the canal and vagina lightly

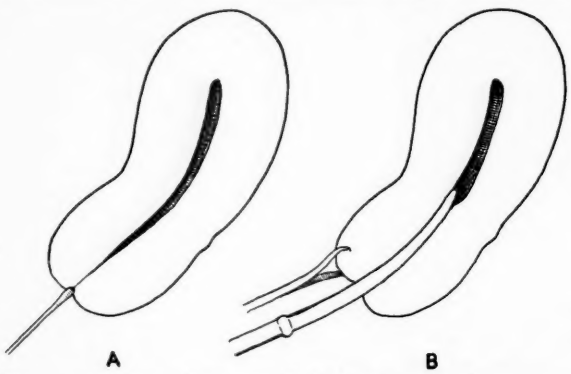


Fig. 14. This patient complained of severe dysmenorrhea and prolonged periods since conization of cervix two years ago. When first seen (A) a probe could barely be forced through the external os and canal. B, anterior lip grasped with tenaculum, external os gradually dilated to admit applicator soaked in 35 per cent cocaine solution. Graduated Hegar's dilators introduced up to No. 8 on first treatment, and to No. 12 on second treatment a month later. Periods painless and of her normal three days' duration since the first dilatation.

with gauze soaked in 1 or 2 per cent mercurochrome solution, which is left in overnight.

The after-treatment is the same as for the other methods, except that it is necessary to dilate the canal regularly during and after healing to prevent stenosis. This method is superior for the deep-seated endocervical infection of long standing.

Although the technique is easily learned, it should not be tried even by the expert gynecologist until he acquires experience with this particular method. I have seen instances of severe stenosis and know of other cases of severe hemorrhage necessitating hospitalization and transfusion. The fault is due not to the method but to its application, for in a large series of his own cases, Hyams reports no hemorrhage, no stenoses, no strictures. Knowledge of the appropriate voltage and amperage to be used is essential. Too great a heat will cause excessive carbonization and subsequent stenosis. Too fast a cutting current will cause hemorrhage. The current to be used should be checked on raw steak before each operation.

In my series of less than one hundred cases, there were four complications. One patient developed an acute pelvic infection principally of the left tube and ovary, mild in degree, which cleared up in two weeks with palliative measures. She had a long standing chronic endocervicitis with no history or evidence of gonorrheal infection nor adnexal disease prior to the conization. Three patients had profuse oozing. These were controlled by tight cervical and vaginal packing which was left in place for forty-eight hours. There were no subsequent stenoses nor strictures.

Jacoby[38] followed up a series of 150 cases, fifty in each group of comparative degree of pathology, who were treated by cauterization, coagulation and conization respectively. Those treated with cauterization were cured more quickly and there was no complication in this group. Nabothian cysts and cervical erosions were best treated by cauterization. Moderate stenosis of the cervical canal occurred in six patients treated by coagulation. Acute inflammation of the tubes and ovaries developed in four patients treated by coagulation, and in three treated by conization. Six patients treated by coagulation had a subsequent period of amenorrhea lasting from three to fourteen months. He concluded that cauterization is superior to electrocoagulation and conization. We heartily concur with him in this conclusion.

Leucoplakia. With a wire loop as the active electrode, the patch with a small circle of its surrounding normal tissue is removed, using a fast cutting current, as for Hyams' conization. The tissue removed is examined microscopically.

Stricture and Stenosis. Prevention is better than cure, and since many cases are due to treatment, one of the important steps is to become experienced with the above methods before undertaking their use. Another point is to follow up cases, especially where canal coagulation, conization or intra-uterine radium treatment has been done, once a month for three to six months, testing the patency and caliber of

the canal. When the patient is seen with stricture or stenosis already present, great improvement is often possible by gentle dilation with Hegar's metal dilators. This can easily be done in the office. (Fig. 14.)

The anterior lip of the cervix is grasped with a tenaculum, the canal cleansed, anesthetized with 35 per cent cocaine solution applied to beyond the internal os. Dilation is gently and gradually started with as small a dilator as is necessary, increasing gradually up to Hegar's dilators No. 12 or 13. It may require several treatments before this size is reached. For strictures we dilate once weekly, and for stenosis once a month just preceding the period. If the stricture completely occludes the canal and cannot be overcome, it passes beyond the realm of office treatment. In acquired stenosis, the relief of dysmenorrhea is immediate and considerable. Usually if the dilation is done before three successive periods, no further treatment is necessary.

I have used this method of cervical dilation immediately preceding the menstrual period for severe primary dysmenorrhea where the internal os is very tight, often accompanied with an acute anteflexion. There are a surprising number of cases which respond remarkably well after three such monthly treatments. The procedure is so simple that it is well worth trying.

SUMMARY

This paper discusses the office treatment of the following cervical lesions: erosions, nonspecific endocervicitis, lacerations complicated by eversion and/or erosion, cysts, polyps, stricture, stenosis, leucoplakia, endometriosis, varicosities, and "strawberry cervix." Cervical anatomy and pathology are reviewed briefly. Accepted methods of office treatment of these lesions are discussed.

CONCLUSIONS

The cervix is the most common source of pathology in the pelvis. Twenty per cent of virgins and nulliparae and 70 to 80 per cent of multiparae are affected.

Cervical pathology is responsible for a considerable amount of discomfort and invalidism. It may cause postoperative and postpartum infections, and is the most important predisposing cause of carcinoma of the cervix.

Physical examination of a woman is incomplete without a pelvic examination including careful inspection of the cervix.

Postnatal care should always include inspection of the cervix, and the period of observation should be six months rather than six weeks.

Topical application as a cure for most cases of cervicitis is inadequate and should be restricted only to that small group where the more effective electrosurgical methods are contraindicated.

Dickinson's method of cauterization with the nasal tip cautery marks the greatest improvement in treatment. It is the simplest in application, gives the best results in the largest number of cases, with a negligible percentage of complications resulting from the treatment.

Electrocoagulation and Hyam's conization are good methods, the latter especially being helpful for the badly infected endocervix with the small os. There is a higher percentage of complications following these methods, even in the hands of experts.

Acute infection of the cervix or other pelvic organs is a contraindication to electrosurgery. Pregnancy is no contraindication, but gentleness should be particularly stressed in this group.

Cervical stricture and stenosis, especially the latter, can usually be overcome by gradual dilation with Hegar's dilators.

The large body of physicians throughout the country could easily acquire the knowledge and armamentarium which would enable them to increase and enlarge their usefulness in the office treatment of cervical pathology.

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THE IMPORTANCE AND METHODS OF SEMEN EXAMINATION IN CASES OF STERILITY

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THE importance of the male rôle in infertile marriages is becoming more and more evident. In part this is due to our better understanding of disturbances of fertility in general, and in part to the more accurate semen appraisal which can be carried out today. It is not many years ago that the male was blamed for an infertile marriage in not more than 10 per cent of all cases, and a semen examination was often not made at all, or at most a glance was given the semen under the microscope; if motile sperms in fair numbers were present, the man was absolved from any blame for the childless marriage. In fairness to the man it must, however, be admitted that if for one reason or another, not apparent to the examiner at the time, the sperms were not motile the patient was often entirely erroneously considered sterile. We know today that a cursory examination of the semen is entirely inadequate and that a man may have many actively motile sperms in his semen and still be infertile. In such cases, however, this infertility can only be determined by a very careful detailed analysis. With such an analysis many "obscure" cases of infertility clear up immediately. I, personally, feel that infertile marriages are as often due to the male as to the female.

For years I have been stressing a 50 per cent male-50 per cent female basis for sterility, and hope to see this recognized at a date not too far off. Already the previous 10 per cent of the cases of sterility ascribed to the male has generally been advanced to 25 per cent, and many other men even believe 40 per cent to be nearer the truth. Plain logic would speak for an equal distribution of the blame in infertile unions, but we also have empirical evidence in the case of animal breeders whose knowledge human medicine neglected, perhaps because man considers himself such a superior animal. It is probably this reason, too, and the male ego which has long prevented the recognition of the male rôle in abortions, a fact well known to animal breeders for a long time.[1,2]

In dealing with human infertility we must first of all be careful to mean what we say. The term sterility is altogether too often used to mean lowered fertility and not sterility. The latter is the state of complete inability to impregnate or conceive, and usually due to such gross factors as absence of the vagina, atrophic testes or ovaries, closed vasa deferentia or Fallopian tubes, etc. Thus problems of diagnosis are generally not created by these cases. It is the disturbance of fertility of lesser degree which creates the diagnostic difficulties. In such cases it is not unusual to see couples who consider themselves sterile, when as a matter of fact the woman conceives from time to time, but aborts spontaneously soon thereafter. These early abortions are then usually interpreted simply as delayed menstrual periods. It is now a well established fact that most spontaneous abortions are due to abnormalities of the zygote. It is often inadvisable, therefore, unless one knows the complete status of both prospective parents, to try every measure possible to save what may turn out to be an abnormal child. This fact I have stressed repeatedly.[3]

Each infertile couple is an individual problem. No man or woman can be judged alone, but only in relation to his or her sexual partner. If we consider the ideal fertility of an individual as 10 (an ideal not present in actual life, especially in more highly civilized countries), then the combined fertility of two such individuals

would be 10 times 10 or 100 per cent. My experience has shown me that clinical sterility is present when the combined family history and whether or not husband and wife were nine months babies. (Veterinarians have shown that under- and over-

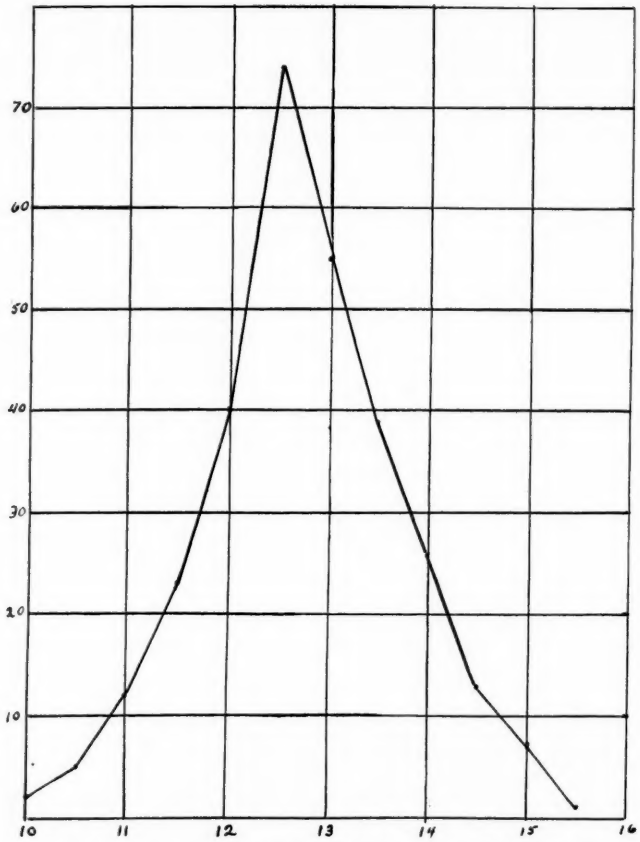

FIG. 1. A quite symmetrical graph of a normally fertile man with good seminal cytology. Coefficient of variability 7.825 ± .215. This graph, like Figures 2 and 3, was made up of the values obtained by measuring 300 sperm heads at a magnification of 3000 diameters in 0.5 mm. The values on the x ordinate are millimeters, those on the y ordinate indicate the observed number of sperm heads of this particular size.

fertility sinks below 60 per cent. Sixty, however, can be made up of various figures (9 times 7, 8 times 8, etc.) and thus one sexual partner can within reasonable limits make up for the infertility of the other. In this way it is easy to explain the formerly puzzling cases of infertile unions which broke up, but later when each partner married some one else, both couples had children born to them. Every sterile couple requires investigation both as individuals and in relation to one another.

The examination must start with a painstaking anamnesis which includes the carried offspring later on are often of poor fertility.) General and special diseases and operations must be asked about, as well as dietary and sexual habits recorded. The breeding record of the couple must be very closely examined, since the birth of a child does not in any manner indicate a satisfactory evidence of fertility, since repetition of intercourse by the same two partners may eventually lead to pregnancy, even if the fertility is rather low.[4]

General and special physical examinations must follow the taking of the history. That endocrine disturbances and abnormal

basal metabolism reactions are very important need not be stressed here, since this is so well known.

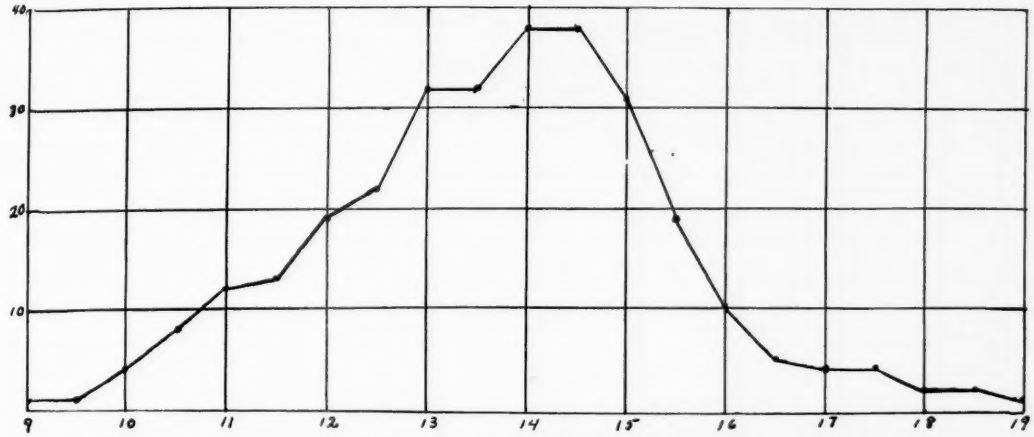

Fig. 2. Graph of a sterile man with poor seminal cytology. Coefficient of variability 12.900 ± .355.

In the case of the male the genitals must be examined for abnormalities. The size of the testes, within reasonable limits, is not so important here as the consistency of the gonads. Soft testes usually indicate disturbed spermatogenesis, but unfortunately the reverse is not true. The prostate and seminal vesicles must also be palpated for determination of size, congestion, inflammation, tenderness, etc.

Following this an examination of the semen is carried out. The best way to obtain this is as a friction specimen produced in the office. For one reason or another it is not always possible to secure such a specimen. Then a specimen as fresh as possible should be obtained, either by intercourse and withdrawal and ejaculation into a clean glass container, or with a condom, providing the semen is taken out of the condom immediately. Preferably this is done by holding up the condom and snipping the closed end at the bottom with a sharp pair of scissors. In this way the semen will come into contact with the minimum amount of rubber.

The semen should then be delivered as soon as possible to the office, being kept cool in the interval at the open window except in extremely cold weather. Too often the semen is kept warm, but we know today that even body temperature acts deleteriously on the spermatozoa and kills all of them, probably in less than twenty-four hours, and certainly in forty-eight hours. This was a paradoxical fact as long as the sperms were considered to be stored in the seminal vesicles, but we know today that the sperms are stored in the tail of the epididymis where they are at a lower than body temperature.[5]

Because of the deleterious effect of body temperature it is not good to leave the tied or twisted condom in the vagina to be brought to the office by the woman. Here a doubly deleterious effect—from the condom and the body heat—is acting. The method of taking semen from a seminal pool in the vagina after coitus is also not good, since, first of all, the presence of vaginal secretion and cells adds to the difficulty of proper semen examination, and if the examination is done immediately after coitus, no knowledge of the action of the vaginal secretion can be obtained. If examination is done, as is usual, after an hour or so, the sperms which are normal should already be up in the cervix and beyond reach of the examiner. Furthermore, we can be certain today that such a condition as sexual incompatibility of a man and a woman does not exist. All the known races of mankind are fertile with one another and produce fertile offspring, so that it is the height of illogic to predicate sexual incompatability between two sexual partners who are most often of the

same race. This hypothesis of sexual incompatibility was evolved for cases not explainable with the former state of our knowledge.

ally of little use to test the seminal hydrogen ion concentration. Unless this is done with very definite precautions the results

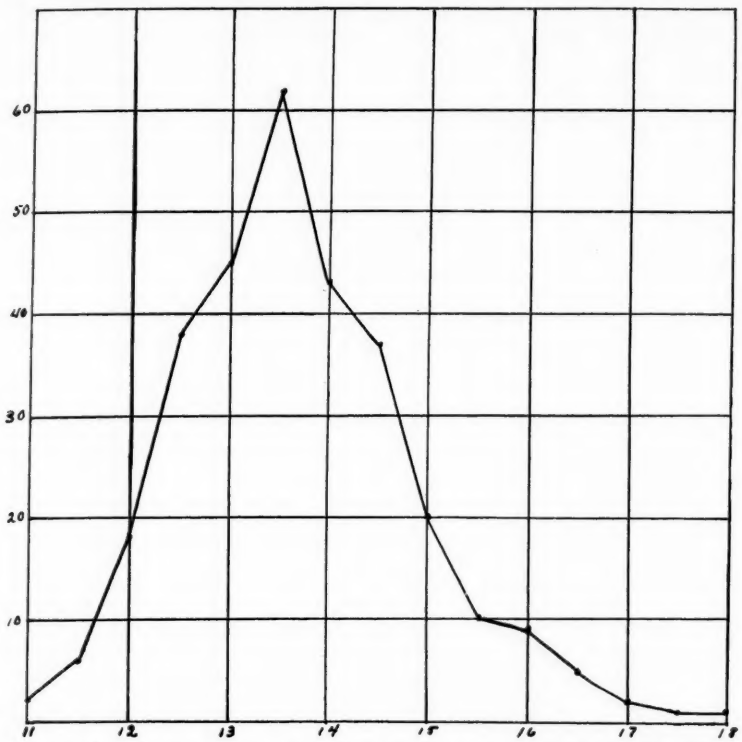

Fig. 3. Graph of a man of very low fertility (practically sterile), with good seminal cytology and a coefficient of variability of only 8.521 ± .239. The skewness factor, however, was 5.62 times the probable error.

After the semen reaches the office it should be examined for quantity, color, turbidity and viscosity. Lessened quantity may mean diminished action of the secondary sex glands, either congenital or acquired, due to disease, endocrine imbalance, age, etc. In normal cases, frequency of intercourse will cause lessened amounts of ejaculated semen. Color and turbidity of the semen will be influenced by blood and pus or diminished prostatic secretion; the latter will often decrease turbidity and viscosity. Increasing age leads sometimes to a gritty semen due to prostatic concretions. Increased viscosity of the semen is due also to diminished amounts of seminal production, due to diminished sex gland activity or frequency of intercourse. Unless markedly increased, viscosity does not have much effect on the fertilizing power of the semen. It is generare valueless, and furthermore, the semen has such a powerful buffer reaction that the hydrogen ion concentration automatically takes care of itself.

A slide of the semen is then made and the number and motility of the spermatozoa observed. Also the presence or absence of blood, pus, and extraneous substances is observed. Since this has been taken up in a previous article in this Journal,[6] I will not go into it here. I only wish to stress that the semen should be observed for five to six hours in every case.

While the fresh semen is being observed, smears of the semen are made on slides, using the technique of making blood smears. These smears should be as even and as thin as possible, except that if very few sperms are present, thicker smears may be used to obviate the extremely tedious labor of counting a sufficient number of cells.

This is, however, but the choosing of the lesser of two evils, as the smears naturally will not be so clear as thinner ones.

The smears are then quickly dried by an air current and passed through the flame just enough to fix them, that is, they should feel only warm to the back of the hand. Depending on the amount of mucus present, the slides are immersed in a 1 per cent chlorazene solution for 15 seconds to several minutes, then washed carefully with distilled water and 95 per cent alcohol. This latter is necessary to prevent precipitation of the alcohol-soluble stain. This stain consists of:

	Parts
Ziehl-Neelsen's carbolfuchsin	50
Eosin (Grübler's bluish alcohol-soluble)	25
Ethyl alcohol, 95 per cent	25

This stain is made up and filtered. When a slide is to be stained, some of the stain is poured into a small dish and carbolfuchsin is added, a few drops at a time, until a metallic film forms on the surface of the solution. The solution is then filtered and used. It is, however, possible to use the stock solution directly if care is used to avoid precipitates by refiltering when necessary.

The stain is spread evenly over the whole slide in adequate amounts to prevent drying and precipitation, and left on three to five minutes. It is then poured off, the slide washed in distilled water, and stained a few seconds with Loeffler's methylene blue diluted 1:4 with distilled water. The slide is then washed again, dried, and examined under the microscope, using an oil immersion lens and a 10× ocular. If the slide is for morphologic studies only, it is well to have a good blue counterstain. For biometrical purposes, however, it is easier on the eyes to keep down the blue color.

It has been repeatedly asserted by some men that my methods of preparing the slides cause artificial sperm changes. This had been checked by me at the very beginning of my investigations and found to be untrue. Since then it has been checked again and again, always with the same results. Furthermore, of the dozens of staining methods which I have investigated, the one described is by far the best, at least in my hands, and I have yet to see slides made by others which are superior to mine. One might also say that if sperm changes are produced by the handling of the smears which allow of a determination of the fertility of the individual, so much the better.

In the morphologic studies the various sperm forms are tabulated as normal, body changes, and head changes. It is the latter which offer the best index of fertility. Head changes are classified as small, large, narrow, tapering, round, heads with overdeveloped end knobs, solid staining and amorphous head forms. (My plates of the various sperm abnormalities have appeared a number of times so that it does not seem necessary to republish them here again.[3a,3c,7])

After one has gotten a general impression of the slide and the average size of the sperm heads in the particular case (they vary somewhat in mean size, even in normal cases), it is not difficult to distinguish between a very large and a very small head, or to pick out long tapering or narrow heads. That, however, is not the crux of the matter. It is evident that there will be gradations of every conceivable type in the sperm head abnormalities, and it takes a large amount of experience to know where to draw the line between normal and abnormal sperm forms. Unless the examiner possesses such experience, which can only be obtained by intensive practical work, his results will not only be unreliable but often entirely erroneous. In such cases even a cursory semen examination would be preferable, as at least it would not lead to complete reversal of the true facts in the opinion of the man or men treating the particular infertile couple.

As an illustration of my point, I may cite a case in which the semen of a man was said to contain very many extremely motile sperms and no abnormal heads (normal—up to 20 per cent abnormal head

forms). Yet the wife, who had been found normal, never conceived. The conclusion drawn by the physician, therefore, was that sperm cytology did not allow of a determination of the fertility of an individual. On account of the importance of the questions involved, I was naturally very much interested. In 1926 I had introduced the detailed semen examination to the medical profession. Since then all my efforts to disprove the assumption that sperm characteristics allow of a determination of the fertility of the individual have failed. On the contrary, a vast amount of evidence has accumulated to support the value of the detailed semen examination. In 1926 I tentatively set 20 per cent abnormal head forms as the dividing line between normal and disturbed fertility. Between 20 to 25 per cent abnormal head forms indicated diminished fertility, and abnormal head forms above 25 per cent usually meant at least clinical sterility within the reservations already mentioned pertaining to human relationships. I builded better than I knew at the time because experience has supported my original figures practically entirely. In all my cases, however, I had never seen a single one with less than 7 to 8 per cent abnormal head forms, and even these were few and far between; 10 to 15 per cent abnormal head forms represented the usual findings.

In view of these facts, I am extremely suspicious of sperm counts purporting to show no abnormal sperm heads or even 2 to 3 per cent of such changes. It was possible later to check the case and 26 per cent abnormal sperm heads were found. It was easy to understand why such a discrepancy was possible, since most of the sperm head abnormalities consisted of size differences, hard to evaluate at the magnification of 1000 diameters which is ordinarily employed. The biometrics corroborated my morphologic count since the coefficient of variability was very high.

Such a case shows the importance of thorough versing in sperm changes. This is just as much a question of morphology as is tissue diagnosis. I frequently receive requests for descriptions of the technique of my method of sperm examination, because some one wants to try it on a case, or have his nurse or secretary do it. This simply cannot be done. These same men without proper training certainly would never attempt to diagnose an early carcinoma of the cervix, or detail their nurse or secretary to do it. Yet on the results of the semen examination depend the further handling of the case and at times the question of operating on the wife.

It is evident also that a simple summation of the number of abnormal sperm heads does not give the complete picture. Different types of sperm head changes have varying significance and the same types of cells in different specimens do not always have the same importance—narrow and tapering sperm heads indicate the greatest disturbance of spermatogenesis, and such disturbance is more or less directly proportional to the number and length of the sperm heads and their narrowness. Thus a sperm head count may show 20 per cent or less abnormal sperm heads and still mean infertility if these narrow and tapering sperm heads total more than 7 to 8 per cent. Again a semen may show the same sperm head count after treatment as before and still be improved, as shown by a shortening of the narrow and tapering sperm heads. Round sperm heads are not of great significance, but become even less important when in this particular semen most of the sperm heads show a tendency toward roundness.

In evaluating a sperm count all these various factors have to be taken into consideration. If the sperm head abnormalities are very numerous one can stop there, since the infertility of the man has been determined. Usually, also, a poor morphologic picture is associated with a poor biometrical result, but this is not necessarily so. Therefore a normal sperm head

count does not absolve the man from all blame for the infertile marriage because many of the sperm head size differences may escape notice in the ordinary morphologic examination, but will be revealed by the biometrical methods.[8]

Biometrics are carried out either by filomicrometer measurements (a very tedious procedure), or preferably by projecting the sperm head images onto a very glossy piece of paper (pinwheel paper) and measuring the length of 300 to 500 sperm heads in 0.5 mm. by means of set screw calipers. A graph is then constructed from these values. The functions of the graphs are determined, and if the coefficient of variability is above 11 or 11.5, disturbed fertility is usually present. It is unfortunately true that even normal morphology and normal simple biometrics do not always indicate fertility. The lopsidedness of the graph obtained must at times also be taken into consideration, since such skewness can only be produced by an abnormal number of small or large sperm heads. If such calculated skewness exceeds four times the probability of error it becomes significant. Such skewness was the only disturbance we could find in a few of our cases, yet the clinical history and course completely verified our calculated results. (Figs. 1, 2, 3.)

While the value of the described detailed sperm examination has been accepted by most men, some have voiced the objections that the seminal picture is not constant, that it is not important whether 85 per cent or 60 per cent of the sperm heads are normal (in cases with 15 or 40 per cent abnormal sperm heads) and that the difference between 20 and 25 per cent (normal limit and sterility) is too small to be considered seriously as a factor in sterility.

These objections are, however, not valid, and are based in part on wrong premises. First of all, except in disease and with age, the seminal picture does remain constant as far as the morphology and biometrics is concerned. This was the first point I had had to determine before I could even attempt to correlate seminal cytograms and fertility. It is true that frequent coitus reduces the number of the sperms, but the morphology always remains constant, except for a slight increase in immature sperm cells, cytoplasmic drops, and an occasional spermatid. Sexual abstinence for some time may increase the number of abnormal sperm forms in the first ejaculate (not after that), since the old dying and degenerated sperms gradually find their way into the seminal vesicles where most of them remain until ejaculation takes place. The constancy of the seminal picture in the same man within reasonable limits of time (that is, avoiding the inevitable onset of increasing abnormalities with age) has again and again been checked by me. Thus a three months' abstinence and daily intercourse for several weeks did not change the seminal morphology or biometrics.

As far as the second objection is concerned, namely that "it is unimportant whether 15 or 40 per cent of the sperm heads are abnormal as long as the other cells are normal," this shows a complete lack of understanding for the basic principles on which the method of sperm examination is based.

It is axiomatic in nature that the crop is dependent on the soil. With a good soil a numerically good crop is obtained, and with pure strains the fruit borne will all be more or less of the same shape and size with certain normal variations. With a poorer soil a poorer crop will be obtained and the shape and size differences will increase. After studying some particular pure strain crop, say Victoria peas, the percentage of the aberrations of size and shape from the normal can be fixed, and it will be found that if the soil is very poor a stage will be reached where none of the peas are fully developed, at least internally, so that even those that look normal to the eye, when planted, will not germinate. By tabulating the variations of size and shape it will be possible to predict this lack of germination in advance. In other words, the externally visible abnormalities are the

recognizable indicator of the degree of disturbance present in the whole crop. In the same way the sperms are the crop of the seminal tubules and the visible abnormalities are simply used in the same way as an indicator. Experience has shown me that when more than 20 per cent of the sperm heads are visibly altered all of the sperms have been affected to some greater or lesser degree, depending on the number of visible abnormalities above 20 per cent and the type of changes. Thus 40 per cent abnormal sperm head forms now means 40 per cent visibly abnormal sperms and 60 per cent also abnormal sperms (here and there one —perhaps one in a thousand—may be normal) but not recognizable with our crude microscopic equipment.

As far as the difference between 20 and 25 per cent goes, this is a difference of 25 per cent. No one, I believe, will have the temerity to deny, for instance, that a 25 per cent difference of thyroid function is insignificant.

Aside from the spermatozoa, semen also contains cytoplasmic drops and cells from the genital tract of the male—urethra, prostate, testicular tubules, etc. Normally the number of these cell forms is not large. But they are important and significant. I have, however, already discussed them in detail and refer the interested reader to the preceding article.[6]

Summing up all the findings discussed so far, then, we see that a number of different seminal pictures are possible. These can be epitomized as follows:

A. Normal cases: semen ejaculate grossly normal, totaling 3 or more c.c. with 60 or more millions of actively motile sperms per c.c. (There is, however, a wide variation of the normal limits both as to the amount of semen ejaculated and the number of sperms per c.c., as pointed out previously.[6]) Very small semen specimens of 0.5 c.c. or less are, however, usually abnormal. There should be 20 per cent or less abnormal sperm head forms with less than 7 or 8 per cent combined narrow and tapering head forms. These should not be of the extreme variety. Double and unripe forms should not exceed 2 or 3 per cent each. The cytoplasmic drops may reach 4 or 5 per cent and cells of spermatogenesis should total not more than 0.5 to 1 per cent.

The biometric results should show a coefficient of variation of not more than 11.0 to, at the most, 11.5. Skewness should not be significant.

B. Sexual overloading in a normal individual, and also temporary disturbances, may and do lead to decreasing numbers of spermatozoa and increasing numbers of cytoplasmic drops, coiled and immature sperms and spermatids, though the latter will still be relatively rare.

C. Sexual hypoplasia of a mild degree will also give a picture similar to the preceding, but later rechecking will allow of a differential diagnosis. In the severer degrees of hypoplasia, of course, more marked abnormalities are seen, down to an ejaculate of only a few c.mm. containing practically no sperm cells and only some testicular spermatogenic cells.

D. Testicular degeneration in a mild chronic form also shows pictures similar to B and C, but here many sperm head abnormalities, especially many long and narrow and tapering sperm heads are seen. Often indeed a complete museum of sperm abnormalities is present. Severer degeneration will show fewer and fewer sperms, more abnormal forms, and more degenerated spermatids, up to a certain point, after which the seminal ejaculate will be small, show few, mainly abnormal, sperms, and practically no cytoplasmic drops or spermatids since spermatogenesis is at a very low ebb. In acute degeneration the whole testicular tubular cell lining may be extruded, often in sheets, depending on the severity of the condition. Sperms will be absent. Later on neither sperms nor cells of spermatogenic origin will be found. This picture is identical with that of bilateral vas obstruction. Testicular puncture will show sperms in the last case, but not in the first.

E. Testicular regeneration—after long continued severe sexual overloading or

following treatment—will give a picture very similar to C. Cytoplasmic drops may equal the number of the sperms and up to 20 per cent of the cells seen may be spermatids. The increasing number of sperms will, however, immediately show the true condition present.

Thus a careful semen evaluation forms a criterion not only of the present state of the patient's fertility, but also to a certain extent gives a hint as to the prognosis. The latter, however, must always be very guarded. Every case is a problem in itself and no guarantees can be given even in apparently identical cases because of our still very great ignorance of endocrinologic disturbances.

Treatment. Since general good health is intimately associated with fertility, good common sense in living is of vital importance. Coitus should be reduced to a feasible minimum. Thyroid is advisable in all cases where the basal metabolism is even slightly low (and it has been low in the majority of my cases). Vitamin E, essential to growing cells, should be given in doses of about a dram a day. In addition, gonadotropic hormones, that is, the follicle-stimulating hormone of the anterior pituitary, should be given. Through the courtesy of Parke, Davis and Company and of E. R. Squibb and Sons I have used antuitrin and gamone extensively with some very good but entirely unpredictable results. Although I have used these drugs, especially antuitrin, for several years, It is still too early for me to make any didactic statements about these products. I will say, however, that were it not for the patients' patience giving out, usually in the short time of a few months, very much better results could have been achieved. Most of my patients have shown at least some improvement. Some have reached a perfectly normal state and have had children, provided the wife was normal. Other cases, however, have been complete failures. Frequently, however, if after three months' treatment the patient's wife was not yet pregnant the treatment would be discontinued in disgust. Often the patient would expect a condition he had had for ten or more years to be cleared up in three or four weeks. No doubt with our steadily increasing knowledge of the endocrines better results will be obtained in the future in cases of spermatogenic disturbances.

There remains only one other question to be discussed and that is the question of operation in men with obstruction of both vasa deferentia. An operation connecting the vas deferens beyond the obstruction to the head of the epididymis is neither difficult nor dangerous, but rather patience-trying on account of the small caliber of the vas. The results of such an operation, even if patency of the vas should remain established, are rather questionable because the sperms only mature as they pass on from the head of the epididymis to the tail; thus most of the sperms after a vasoepididymostomy will be immature. The same objection can be raised against the attempt to produce pregnancy by injecting into the cervical canal sperms obtained by testicular puncture. Besides, only very few, slightly motile sperms can be thus obtained. However, the literature does contain some cases in which such measures resulted in pregnancy.

CONCLUSIONS

Summarizing the present article and also the one which appeared in the March issue of this Journal the following conclusions seem warranted:

1. Every infertile couple presents an individual problem which can only be assayed if both partners are properly investigated since the fecundity of the couple depends on the relative fertility of one partner to another.

2. The fertility of the man depends more on the qualitative than on the quantitative production of spermatozoa.

3. Motility of the spermatozoa must be evaluated very carefully as there are many, almost imponderable, sources of error which may lead to entirely erroneous conclusions.

4. The informative value of the detailed semen examination seems to be well established today. Apparently contradictory reports so far have been shown to be due to improper interpretation of the seminal findings. This but emphasizes the fact that the proper recognition of the various abnormalities in the seminal cytogram is a morphologic problem which requires detailed training and experience. It is generally true that sperm head abnormalities totaling more than 20 per cent indicate at least some disturbance of fertility. There are, however, exceptions to this rule and a simple summation of the sperm head abnormalities does not show the whole picture. Aside from the spermatozoa themselves the other cells of spermatogenesis are important for the complete evaluation of any semen specimen.

5. As a rule sperm morphology and biometrics run parallel, but this is not necessarily so. Usually a graph with a coefficient of variability above 11.0 to 11.5 indicates a disturbance of fertility, but in some cases both the seminal cytogram and the simple functions of the graph may be normal while a disturbance of fertility is indicated by a marked skewness of the graph.

My experience over the years has shown me that if all the points mentioned are given due consideration, unexplained cases of sterile marriages will be decidedly rare. However, it must not be forgotten that repetition of intercourse may lead to conception even in cases with low fertility. The occurrence of such conception may be seen at any time and is entirely unpredictable. A recognition of this fact will explain some otherwise apparently paradoxical cases. The rôle of the male in abortions must also be remembered.

Therapy of disturbed spermatogenesis is still in its infancy. In my hands the best results were obtained with the follicle stimulating or spermatogenic factor of the anterior pituitary gonadotropic hormone.

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* For a more complete bibliography see the March, 1940 number of this Journal, page 586.[6]

CHRONIC SUBINVOLUTION, CHRONIC METRITIS AND HYPERTROPHY OF THE UTERUS*

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CHRONIC subinvolution was accurately described by Fletcher Shaw as early as 1914. Before this the term fibrosis was applied to many benignly enlarged uteri. In spite of this, modern textbooks discussed the condition very vaguely, if at all. In 1918, the writer confirmed the work of Shaw, but the subject, important as it is, received very little attention in the literature. As late as December, 1938, the author reviewed the subject before the Baltimore Gynecological Society, and the discussion that arose pointed out clearly that comparatively little was known generally about this rather common gynecologic lesion. To give an idea of the frequency of the condition, one needs only to quote routine laboratory figures. Since 1919 we have routinely stained every uterine section with hemotoxylin and eosin, and orcein Van Gieson, classifying them as normal, chronic subinvolution, chronic metritis, hypertrophy and diffuse adenomyosis. Since the return of Gynecology to Obstetrics at Washington University School of Medicine in 1929, this routine was continued and the following figures give one an idea of the frequency with which these various lesions were met as compared to the frequency of myomata.

Number of specimens from July 1, 1929 to July 1, 1939	11,483
Chronic metritis	262
Adenomyosis of uterus	586
Chronic subinvolution	583
Hypertrophy of uterus	9
Myoma of uterus	1,632

It will be noted that clear-cut hypertrophy occurred only nine times. These lesions are definitely forerunners of diffuse adenomyosis, the invasions of the musculature taking place after the presence of hyperplasia of the endometrium and hypertrophy of the wall.

CHRONIC SUBINVOLUTION

Although the characteristic features of the changes of distribution of elastic tissue in a parous uterus have been described for some time by numerous writers, the clinical diagnosis of chronic subinvolution was not definitely suggested until the work of Fletcher Shaw as late as 1917. Before this time the term "chronic metritis" was often applied to a definitely enlarged uterus which was associated with retroversion, pain and hemorrhage. The term "chronic metritis," naturally, suggests inflammation, and in chronic inflammatory processes there is frequently an increase of connective tissue present. Thus the term "fibrosis uteri" developed and was freely applied to all symmetrically enlarged uteri in the absence of newgrowth. Fletcher Shaw pointed out that these enlarged uteri were most commonly due to changes which were characteristic of subinvolution. He described the pathologic changes of a uterus affected with chronic subinvolution, chronic metritis and also gave us a clear picture of hypertrophy of the uterus. In this study he pointed out that these three conditions could exist as separate entities, but the picture was often confused because of the overlapping of these conditions, that is to say, one or more of these lesions could be present in the same uterus. In 1918, the writer confirmed Fletcher Shaw's work and pointed out clearly that subinvolution was the most frequent lesion found in these enlarged uteri, but that the picture was sometimes difficult to describe because of

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the distinct overlapping of these above mentioned conditions.

Although the pathology of these benign lesions of the uterine wall has been well described, they have received comparatively little clinical attention, and I thought it might be interesting to discuss this subject again and compare our present findings with those of previous studies made a good many years ago.

The best descriptions of the constituents of the normal nulliparous uterus, pregnant uterus and the processes of involution as well as the changes due to subinvolution, in our opinion, are those of Fletcher Shaw. Although these descriptions were made in 1917, they have never been fully emphasized in our American textbooks on gynecology. As they have a definite practical bearing, I shall review these changes here, taking the liberty to quote freely from the previous work of Fletcher Shaw, which we confirmed several years ago.

The Virgin Uterus. Elastic tissue is found as the internal elastic membrane of the arteries. Fibrils of elastic tissue are also seen in the media and adventitia of the vessels. In the myometrium, elastic fibrils are located in between the muscle bundles, not conspicuously in the inner third, but more prominently in the subperitoneal area. There is no definite elastic interna of the veins. More elastic tissue, however, is present in the wall of the veins between the muscle tissue. Elastic tissue is very strikingly seen in the outer portion of the veins, and although not in the form of a membrane, it is sometimes referred to as the external elastic membrane.

Uterus during Pregnancy. All constituents of the uterus are increased. Muscle cells are enormously enlarged. There is an increase in fibrous and elastic tissue, the proportions of these structures being the same as in the normal nulliparous uterus. Marked enlargement of blood vessels occurs in order to take care of the growing organ and convey the necessary amount of blood to the fetus. All vessels are enlarged, but the most striking increase in size is naturally seen in the subplacental site. In the involution of the puerperal uterus, the most marked atrophy known occurs. This process is often referred to as "atrophy acutissimus." The uterus, just after delivery, weighs approximately 1000 Gm. In three or four weeks, it is reduced in weight to from 4 to 6 ounces. This reduction in size is due chiefly to the diminution in size of the individual muscle cells by proteolytic processes within the cell wall. Some fatty degeneration is seen, but this is not conspicuous. There is also some total destruction of cells. Marked changes in the vessels take place, leading to their reduction in size or complete obliteration with marked degeneration of the walls of the arteries of the inner third of the uterine wall. Some vessels are closed either completely or partially by thrombi. There is a marked thickening of the intima of the arteries. The media of the vessel becomes markedly swollen and the internal elastic membrane undergoes vitreous degeneration (the term is suggested by Goodall). In this process the internal elastic membrane becomes greatly thickened and at various stages of this degeneration the staining properties with orcein or Weigert's and Van Gieson stain, vary. From the normal black-brown stain, it goes into a brick red, then a bright red, and finally, as absorption is about to take place, it stains only a faint yellow. The various stages of these degenerative changes can be seen in the same vessel.

The elastic fibers in the media go through a similar process. The adventitia also undergoes hyaline change as does the fibrous tissue of the media. The vessel now consists of a more or less conglomerate mass without any lumen or with a small opening remaining, through which the smaller new vessel subsequently develops. With the development of the new vessel in the patent area of the old, we see the new vessel surrounded by a degenerated structure, which if involution is complete, will be entirely absorbed. If during the process of involution, the vitreous degeneration stops and absorption does not take place, the

degenerated tissue regains the property of staining like normal elastic tissue. Thus, if this process is markedly hindered, we see numerous collars and pads around the newly formed arteries of the inner third of the uterine wall. In the larger arteries, the same process occurs as in the smaller ones, with the exception that the process consists chiefly of the development of a new internal elastic membrane and a new intima, the rest of the old wall remaining intact.

In the veins the walls become swollen due to marked hyalinization of the connective tissue with the compression of the muscle cells. The elastic tissue here also becomes very much swollen, but is so intermingled with the hyaline mass that it is not so distinctly seen as in the case of the arteries. If involution is complete, the hyaline mass is absorbed and new muscle cells develop. If the involution is not complete, the spaces between the muscle bundles of the vein contain the degenerated hyaline tissue, which regains the ability likewise to take the same stain as normal elastic tissue.

Elastic and fibrous tissue in between the walls of the muscle bundles undergoes changes similar to those described for the veins and arteries. This is especially true in the outer portion of the uterine wall. If these degenerated masses are not completely absorbed they regain the property of staining with orcein or Weigert's stain and appear as dark brown degenerated masses of tissue between the muscle bundles.

In the ordinary process of involution the absorption of the degenerating tissue is fairly complete, but there is usually sufficient lack of absorption of these structures around the arteries, in the veins and between the muscle bundles to differentiate a parous from a nulliparous uterus. If the absorption of these degenerating areas is checked, the characteristic picture of subinvolution comes into existence, namely, dark staining collars and pads around the arteries, unabsorbed dead elastic tissue in and about the veins, and similar tissue between the muscle bundles of the outer third of the uterine wall.

PATHOLOGY OF HYPERTROPHY OF THE UTERUS

Hypertrophy of the uterus almost invariably is associated with a marked hyperplasia of the endometrium with a history of prolonged menorrhagia. The uterus is enlarged, chiefly due to a work hypertrophy, the musculature trying to rid the cavity of the excessive formation of the endometrium. Some authorities believe that the hypertrophic condition of the musculature is a primary thing, associated with the hyperplasia of the endometrium resulting from some abnormal overstimulation. This may in part be true, but as one sees hyperplasia of the endometrium frequently without hypertrophy of the wall, one must conclude that the hypertrophy develops secondarily as a work hypertrophy in an attempt on the part of the uterine wall to rid itself of the thickened mucosa. Muscle tissue and fibrous tissue occur in the same proportion as in the virgin uterus. The musculature in the gross appears coarser; this is due chiefly to hypertrophy of the individual cells. The muscle cells stain well and are increased in size rather than in number. In comparing the two fields, one in the hypertrophic uterus and one in the normal nulliparous uterus, the average shows that the fields in the hypertrophic uterus contain approximately three-fifths as many cells as similar fields in the nulliparous uterus. There is perhaps also some hyperplasia of the muscle cells, but this is difficult to determine. The coarser structure is evident microscopically and there is no evidence of infection or subinvolution.

CHRONIC METRITIS

Chronic metritis results from previous acute infection and is invariably seen as an extension of a chronic endometritis. A chronic endometritis is usually established secondarily to chronic salpingitis which in over two-thirds of the cases is primarily of

gonorrheal origin. Chronic metritis may also result from an acute process after abortion or in the puerperium, but not more than 10 to 15 per cent of the cases of chronic metritis are of this origin. A symmetrically enlarged uterus which may be associated clinically with pain, hemorrhage and leucorrhea; the pure chronic metritis type is present in not more than 15 per cent of such uteri removed at operation. The uterus is moderately enlarged. The cut surface is smooth in contradistinction to chronic subinvolution where the surface is uneven due to numerous thickened blood vessels appearing above the cut surface. Histologically there is a marked increase in connective tissue throughout the uterus, strikingly seen in the outer third of the wall, with a diffuse round cell infiltration throughout the thickness of the uterine wall and a tendency of the cells to group themselves around blood vessels and lymphatics.

Wilfred Shaw reinvestigated this subject in 1929. He feels that he cannot support the views of Goodall concerning the involution of the circulatory system of the uterus. He believes that the vessels of the uterus are reduced in size through atrophic changes in the walls which, in the case of the veins and sinuses, are peculiar in that a hyaline degeneration first occurs. The reduction of the lumen is mainly determined by proliferation of the subendothelial tissues. From our own observations in the past, we are more inclined to support the views of Goodall than those of Wilfred Shaw.

Shaw states that the elastic tissue content of the uterus is invariably increased after each puerperium, so that the uterus of a multipara who has borne many children always contains a large amount of elastic tissue. He regards this process as physiologic and does not consider that it determines the condition of chronic subinvolution.

It might be stated that the existence of degenerated tissue around the arteries of the inner third of the uterine wall varies in amount in different uteri. In some instances these complete or partial collars around the artery are abundant and in other instances they are only seen inconspicuously. This would indicate, in my opinion, that they represent a residual condition and in no manner represent newly developed elastic tissue. The same can be said of the large plaques of tissue in the outer portion of the veins and in between the muscle bundles of the outer third. In a normal nulliparous uterus, the elastic tissue is found in fine strands. Newly developed elastic tissue in no way differs in character from this. I, therefore, consider the elastic staining substances as areas of degenerated tissue which have not been absorbed and, therefore, must be considered pathologic if present in any great degree, representing the picture characteristic of chronic subinvolution.

In a previous study, using the Fletcher Shaw classification in the examination of eighty uteri, I classified as subinvolution, thirty-eight; as chronic metritis, thirteen; as chronic subinvolution and chronic metritis combined, nine; hypertrophy, four; normal, eleven; and, senile, three.

I thought it might be of interest to go over a similar series to see how the present observations would classify these enlarged uteri. As a matter of fact, this classification was used routinely in specimens removed at operation. In a recent series, they were grouped similarly, but also included as a fourth lesion, the condition of diffuse adenomyosis. There were one hundred uteri and a diagnosis of chronic subinvolution alone was made in thirty-two cases; chronic metritis in eleven; hypertrophy in two; and, adenomyosis in four. The interesting feature of the study was the frequency of the overlapping of the above-mentioned conditions.

The combination of subinvolution with adenomyosis was found in eleven uteri; that of adenomyosis with hypertrophy in ten; chronic metritis with subinvolution in seven; chronic metritis with adenomyosis in four; and, chronic metritis and subinvolution combined with adenomyosis was found eight times. Other combinations also

existed, but to a lesser degree. We went over the sections separately and were especially impressed by the common association of early diffuse adenomyosis in these specimens.

Schwarz and McNalley previously called attention to the frequency of adenomyosis developing in the wall of uteri pathologically enlarged and considered the above mentioned pathologic conditions to have definite bearing on the development of so-called diffuse adenomyosis.

It is also interesting to note that in over 90 per cent of the cases where tubes were removed, chronic metritis was associated with chronic salpingitis, indicating that chronic metritis, per se, is comparatively uncommon.

Clinically the uterus reaches a fair state of involution, so far as size is concerned, by the eighth week postpartum. That is to say, it is almost the size of a normal multiparous uterus. The complete circulatory changes take somewhat longer and may take two or three months or longer until they are completed. I have always emphasized, in the prevention of subinvolution, that an examination be made between four and six weeks postpartum, preferably four, and that the position of the uterus be noted. If it is retroverted, irrespective of what its previous position was, for the individual, the uterus is brought forward and a properly fitting Smith pessary inserted. The patient is usually requested to return in a week or two and it is surprising to see what a marked reduction in size is obtained in a period as short as a week. I feel that the postpartum uterus in a position of third degree retroversion favors a chronic pelvic congestion and as a result interferes definitely with involution of the circulatory system. The pessary should be worn at least six months, being removed at proper intervals for cleansing. Whether the uterus stays forward or not permanently, is not of so much importance. The more important thing is to keep the uterus in the proper forward position during the first six months postpartum, thus leading to more complete involution. I, therefore, feel that such a procedure, properly carried out, should lessen to a great extent the condition of chronic subinvolution. This condition by itself, in later years, can cause pain and hemorrhage and can lead to the development of other pathological lesions of the uterine wall. Hyperplasia of the endometrium itself, near the menopause as well as at other times, causes marked uterine bleeding. When associated with chronic subinvolution, this sign is often exaggerated.

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BOOK REVIEWS

MANUAL OF UROLOGY. By R. M. LeComte, M.D. Second Edition. Baltimore, 1939. Williams and Wilkins. Price $4.00.

Since the first edition of this manual was published in 1935 so much progress in urology has taken place that the author found it necessary to rewrite practically the entire book. Sections on the neuromuscular physiology and pathology of the bladder and a chapter on impotence and sterility have been added. The author tells us, however, that inasmuch as these subjects are the basis of so much discussion and controversy they "may have to be changed soon, perhaps before this edition is out of the press"—refreshing frankness. This short book (295 pages) is an excellent introduction to the subject, which the student will do well to study before moving on to the larger textbooks and detailed monographs.

OFFICE GYNECOLOGY. By J. P. Greenhill, M.D. Chicago, 1939. Year Book Publishers. Price $2.50.

Greenhill has written a compact, to the point, conservative, up-to-date volume, covering the office procedures in gynecology, and these alone. He has covered the field from the taking of the patient's history, to the gynecologic examination, gonorrhea in adults, the Rubin test, Elliott treatment, backache, vaginal douches, sterilization by coagulation of the uterine cornu, local anesthesia in the office, endocrinology, senile vaginitis, office urology, premarital examination and advice. The book is well written, 406 pages long, has a few necessary illustrations, and an index.

SURGERY OF THE EYE. By Meyer Wiener, M.D. and Bennett Y. Alvis, M.D. Philadelphia, 1939. Saunders.

The authors wrote this volume "to supply a handy atlas for the practicing ophthalmologist and student of ophthalmology [to which they] can quickly refer for information on the surgical correction of ocular defects and disease." It is not a reference work containing every known method or suggestion, but only those procedures are offered which will *best* serve the purpose.

This work purposely leaves little to the descriptive text and imagination. An attempt has been made to illustrate in detail each operation selected. The artist, Dr. A. J. Hofsommer, sketched from actual scenes. The illustrations are numerous (396) and good.

CANCER OF THE COLON AND RECTUM. By Fred W. Rankin, M.D. and A. Stephens Graham, M.D. Springfield, Illinois, 1939. Charles C. Thomas. Price $5.50.

Rankin and Graham have produced a comprehensive and up-to-date record of their experiences covering cancer of the lower gastrointestinal tract. The work of other surgeons in the field, both in this country and abroad, has been correlated and recorded. The book (358 pages, with nearly 150 illustrations) is a most complete presentation of the subject by recognized authorities.

THE RECTUM AND COLON. By E. Parker Hayden, M.D. Philadelphia, 1939. Lea & Febiger. Price $5.50.

Dr. Hayden's book deals with the general subject of diseases of the rectum and colon, omitting unnecessary and nonessential details. The text is based largely on the author's personal experience, augmented by that of several co-workers at the Massachusetts General Hospital, where a clinic was organized to facilitate the diagnosis, treatment, and aftercare of these disorders. For the most part the book deals with the surgery of the rectum and colon. The preparation of the patient, the details of the technique of the various operations and the after-treatment are fully described. The text is richly illustrated with photographs and drawings, especially prepared for this volume.